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EPIDEMIOLOGICAL STUDY ON TUBERCULOSIS IN KOLIN DISTT OF CZECHOSLOVAKIA.

(FIRST & SECOND REPORTS)

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Epidemiological and Clinical Study of Tuberculosis in the District of Kolín, Czechoslovakia*

Report for the First 4 Years of the Study (1961-64)

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Many developed countries are faced with the problem of reorganizing their tuberculosis-control programme to bring it into line with modern conditions. The study reported was undertaken to provide guidelines for this reorganization. It was begun in the district of Kolín, Czechoslovakia, with a population of some 100 000, in 1961 and is still in progress. The paper covers the first 4 years of the study.

In 1961 a thorough check-up was made on all persons registered as having active or inactive tuberculosis or fibrotic lung lesions. In 1961 and 1963 a mass X-ray and tuberculin-testing campaign, with 95% coverage, was carried out for all persons over 14 years of age. All persons with active tuberculosis received adequate treatment. Persons registered as having tuberculosis or suspected tuberculosis were subjected to regular photofluorographic and bacteriological investigations. Newborn infants were given BCG vaccination, and persons aged 14 years and 19 years with negative tuberculin reactions were vaccinated.

The prevalence of bacillary tuberculosis fell from 150 cases in 1960 to 91 in 1964, mainly owing to a decrease in the number of chronic cases. The incidence of bacillary tuberculosis detection by direct smear microscopy, however, remained at about 25 cases throughout the period 1961-64. The risk of developing tuberculosis was found to be highest in persons with fibrotic lung lesions or inactive tuberculosis, and in men above 45 years of age and women above 65 with previously normal photofluorograms.

It is concluded from the study that in developed countries priority should be given to adequate treatment of all persons with active tuberculosis, and to early diagnosis in persons consulting physicians and in the high-risk population groups.

I. INTRODUCTION

BACKGROUND OF THE STUDY: TUBERCULOSIS CONTROL IN CZECHOSLOVAKIA[4]

The epidemiological situation as regards tuberculosis soon after the end of the Second World War was very unfavourable in Czechoslovakia, as indeed in the majority of European countries. Statistical data for this period are incomplete, the most accurate being those on mortality. In 1946 the reported tuberculosis mortality amounted to 127 deaths per 100 000 inhabitants, one of the highest rates in Europe: the gravity of the situation is borne out by the tuberculosis mortality for children up to 15 years of age, which was 44.6 deaths per 100 000 children.

The first relatively accurate information on the epidemiology of tuberculosis was supplied by the tuberculin testing of more than 3 million persons—the majority aged from 1 to 20 years—which was

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[4] Czechoslovakia covers an area of 127 870 sq. km. According to the census of 1 March 1961, there were 13 745 770 inhabitants.

done as part of the mass BCG vaccination campaign carried out in 1948-49. The prevalence of infection was very high: at the age of 15 years, 48% of the persons investigated were tuberculin reactors, and at 19 years of age as many as 67%.

A systematic fight against tuberculosis was inaugurated in 1948, when the tuberculosis clinics—which up to this time had been financed by voluntary organizations—became part of the National Health Service and the cost of treating all patients suffering from tuberculosis was taken over by the state within the framework of the established national health insurance; soon afterwards the preventive and therapeutic programmes were integrated. Among further important measures taken about this time, specially favourable payment of sickness benefits for tuberculosis patients may be mentioned.

The mass BCG vaccination campaign of 1948-49 resulted in the vaccination of 2 188 562 persons between the ages of 1 and 20 years. BCG vaccination of the newborn and revaccination of persons up to the age of 30 years has been compulsory since 1953. By the end of 1960, over 6 million vaccinations and revaccinations had been carried out (see Fig. 1). Czechoslovakia is thus now among those countries with a systematic, high-coverage BCG vaccination programme (over 98% coverage of newborn babies since 1961); this is made possible by the fact that practically all children have been born in hospital during the past decade.

In spite of the measures taken, the epidemiological situation as regards tuberculosis was still serious in the mid-1950s, as can be seen from Appendix Table 1; for example, the mortality from tuberculosis of all forms in 1954 was still 48.8 per 100 000 population, while the prevalence of known bacillary tuberculosis amounted to 195.5 per 100 000 population. The number of newly notified cases of tuberculosis and relapses was altogether 183.2 per 100 000 inhabitants, and 91.4 per 100 000 children. In order to achieve more marked progress in tuberculosis control, in 1955 the Government issued a programme of further measures considered indispensable for tackling the whole tuberculosis problem. Among other things, the bed capacity for treatment of tuberculous patients was further extended; another 100 photofluorography units were purchased; a programme was worked out for the control and eradication of tuberculosis in cattle; and certain new social welfare benefits were secured for tuberculous patients.

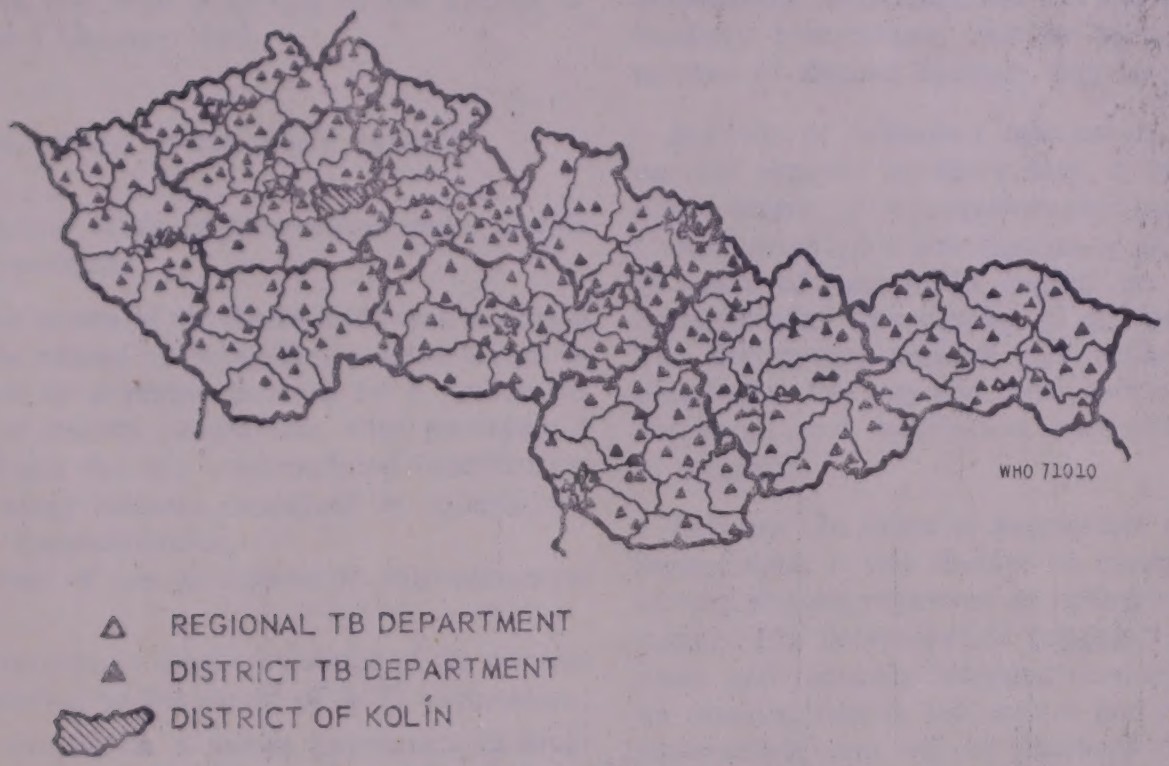
Appendix Table 2 gives a short survey of the personnel and material available for tuberculosis control in Czechoslovakia in the period 1954-63.

FIG. 1

VACCINATION STATUS OF PERSONS AGED 0-30 YEARS IN KOLÍN DISTRICT, 1961

FIG. 2

DISTRIBUTION OF TUBERCULOSIS DEPARTMENTS IN CZECHOSLOVAKIA, 1963



The tuberculosis departments of the polyclinics provide ample coverage for the whole country, as may be seen from Fig. 2. The number of tuberculosis specialists, the number of beds reserved for tuberculous patients and the number of bacteriological and photofluorographic investigations were rather high according to current views, being based on the experience gained in the 1950s. The number of beds and specialists began to show an appreciable decline in 1963, this decline being continued in 1964 and 1965 (not shown in the table).

As a result of the improved services, tuberculosis mortality declined from 48.8 per 100 000 inhabitants in 1954 to 19.0 per 100 000 in 1963, i.e., by 61%. In 1963 the great majority of those dying from tuberculosis were over the age of 60 years. The tuberculosis mortality for children in Czechoslovakia is now one of the lowest in the world. It is also significant that the prevalence of bacillary tuberculosis declined from 211.1 per 100 000 inhabitants in 1957 to 81.9 per 100 000 in 1963, i.e., by 61%, even though the number of bacteriological investigations increased substantially during the same period. The number of newly notified tuberculosis cases together with relapses was 201.2 per 100 000 inhabitants in 1957, and only 127.7 per 100 000 in 1963. As may be expected, the decline is still more marked as regards children (for this same period, from 80.7 to 20.4 per 100 000 children 0-15 years of age). The very favourable situation as regards tuberculosis in children is borne out by the very low incidence of tuberculous meningitis—310 cases for the whole country in 1954 (8.8 per 100 000 children) and as few as 15 cases in 1963 (0.4 per 100 000 children).

The great changes in the epidemiology of tuberculosis in the 1950s demanded re-evaluation of the methods used for tuberculosis control. The main problems were the effective screening for persons with active tuberculosis, the provision of adequate therapy on a national scale, and safeguarding the population so far not infected with tuberculosis. It goes without saying that the aim was to obtain optimum results in as short a time as possible, without excessive expense.

Czechoslovakia therefore agreed to collaborate with WHO in a complex long-term experimental, epidemiological and clinical study of tuberculosis in a representative sample of the population. The study was initiated by Dr L. Šula, then Chief of the WHO Tuberculosis Research Office in Copenhagen. It was planned as a tuberculosis control project, based on the experience gained in the reorgan-

ization of tuberculosis control in Czechoslovakia and in other Member States of the World Health Organization, and has been operating in the district of Kolín since 1 October 1960.

OBJECTIVES OF THE KOLÍN PROJECT

Epidemiological study of tuberculosis under routine control conditions

The main object of the Kolín study was to obtain an accurate picture of the epidemiological trends in tuberculosis in a region covered by a permanent tuberculosis control programme, thus providing a scientific basis for any contemplated modification of the strategy hitherto employed in tuberculosis control in Czechoslovakia.

The points of special interest in this connexion were:

(*a*) the tuberculin sensitivity status of the population, in relation to the extent of BCG vaccination;

(*b*) the prevalence of active pulmonary tuberculosis, in particular of bacillary tuberculosis; the proportion of the prevalence due to chronic bacillary excretors is specially significant;

(*c*) the incidence of active pulmonary tuberculosis, in particular of bacillary tuberculosis;

(*d*) the incidence of relapses;

(*e*) the time trend of mortality from tuberculosis.

Tuberculin testing and BCG vaccination. As mentioned in the previous section, nation-wide tuberculin testing in 1948-49 showed that a large proportion of the inhabitants of Czechoslovakia gave positive tuberculin reactions, i.e., were presumably infected with tuberculosis, and that this proportion increased sharply with age. Since 1953, BCG vaccination of infants at birth and revaccination of persons up to 30 years of age has been compulsory. It was to be expected that vaccination would interfere with the natural tuberculin sensitivity patterns in the lower age-groups. It was therefore decided to compare tuberculin sensitivity patterns in vaccinated and unvaccinated groups, and further to investigate to what extent quantitative tuberculin testing was of value in indicating trends in the epidemiological situation.

Prevalence of pulmonary tuberculosis. In order to provide reliable estimates of the prevalence of active pulmonary tuberculosis, it was decided to carry out a thorough bacteriological investigation of all persons with photofluorographic or other evidence suggestive of pulmonary tuberculosis. This allowed valuable information to be obtained on the prevalence of bacillary tuberculosis, and in particular on the number of chronic bacillary excretors.

Incidence of pulmonary tuberculosis. In order to provide accurate incidence data, it was decided to obtain several point-prevalence estimates by repeated photofluorographic investigation of all persons over 14 years of age—again backed up by thorough bacteriological investigation of all suspected cases. The discrepancy between the incidence estimates obtained in this way and those obtained by routine diagnostic and notification methods was to be investigated.

Relapses. In order to supplement the epidemiological data, it was decided to record all relapses among persons registered as having inactive tuberculosis. The prevention of relapses by early diagnosis and correctly managed chemotherapy forms an essential link in the control and elimination of tuberculosis, and will be discussed further below.

Mortality. Accurate records of mortality were to be kept, in order to reveal any changes in the death rate due to tuberculosis.

Study of the epidemiological impact of mass treatment

The adequate chemotherapy of tuberculosis is today generally recognized as an important part of an effective tuberculosis programme—according to some authors (Canetti, 1962; Crofton, 1960, 1961), even as the most important. The excellent results which can be achieved by uninterrupted long-term combined chemotherapy have been repeatedly found in all countries where this type of treatment can be properly organized.

One of the objects of the Kolín project was to ascertain how far the principles of adequate chemotherapy can be applied to all patients discharging tubercle bacilli in a geographically limited area, regardless of whether these persons are suffering from newly detected tuberculosis or a relapse of the disease or are chronic excretors of bacilli. Great emphasis was laid on preventing cases of tuberculosis from becoming chronic, which forms one of the most serious contemporary problems in tuberculosis control all over the world, not only from the epidemiological but also from the therapeutic, social and economic viewpoints.

When planning the scheme of treatment at the beginning of the study (in 1960) we based our considerations on the situation in an economically advanced country, with on the one hand a sufficient number of beds for tuberculous patients, an adequate number of phthisiologists, sufficient antituberculosis drugs and satisfactory social security for all patients and their families; on the other hand, however, it was necessary to achieve the best possible results without undue expense. In addition, the method of treatment employed for the study had to be applicable to the country as a whole. The therapy scheme was based on an initial short term of hospital treatment, during which period application of antituberculosis drugs can easily be supervised, and a longer period of ambulatory treatment with self-administration of the drugs.

The therapeutic requirements were set at the achievement of long-term bacteriological quiescence in at least 95% of all newly notified cases of bacillary tuberculosis, with a relapse rate not exceeding 0.5% annually.

Determination of the main groups at risk

In countries possessing an integrated tuberculosis-control programme, the discovery of population groups exposed to a higher risk of developing active tuberculosis than the rest of the population is assuming an ever-increasing significance. Tuberculosis incidence appears to be the most useful criterion here. However, the exact incidence can only be determined by complex long-term epidemiological studies; analysis of routine tuberculosis-control records is well known to provide the data on the number and distribution of newly notified cases differing from the true incidence.

The study described here has elucidated the influence of the following factors on the risk of contracting tuberculosis:

(*a*) age and sex,
(*b*) presence of fibrotic lesions in the lungs,
(*c*) BCG vaccination,
(*d*) increase in tuberculin allergy,
(*e*) contact with sources of human infection, and
(*f*) contact with sources of bovine infection.

The planned third mass investigation of the population over the age of 14 years in 1966 will provide accurate epidemiological data for a period of 6 years, thus enabling the groups at risk to be established with greater precision.

ORGANIZATION AND EXECUTION OF THE PROJECT

After 18 months' preparation, the study was commenced on 1 October 1960, using standard procedures recommended by WHO.

The study is being carried out by the Czechoslovak Ministry of Health in collaboration with WHO. The tuberculosis departments of the polyclinics at Kolín and Český Brod, and the tuberculosis sanatorium at Kostelec nad Černými Lesy (n.Č.l.), are the main tuberculosis control centres involved. Both tuberculosis departments are staffed with 2 full-time and 1 half-time tuberculosis specialists, 7 clinic nurses, 3 BCG nurses, 1 X-ray technician and 1 administrative worker. Bacteriological investigations for the tuberculosis departments at Kolín are carried out by the district laboratories of the public health service and at Český Brod by the tuberculosis sanatorium at Kostelec n.Č.l.

Additional personnel for the study—7 physicians (phthisiologists, epidemiologists, research workers), 3 X-ray technicians, 2 BCG nurses, 3 qualified medical auxiliaries, 1 statistician, 5 clerks and 2 drivers—were made available by the Tuberculosis Research Institute, Prague, the Institute of Epidemiology and Microbiology, Prague, and the Regional Institute of National Health, Central Bohemia.

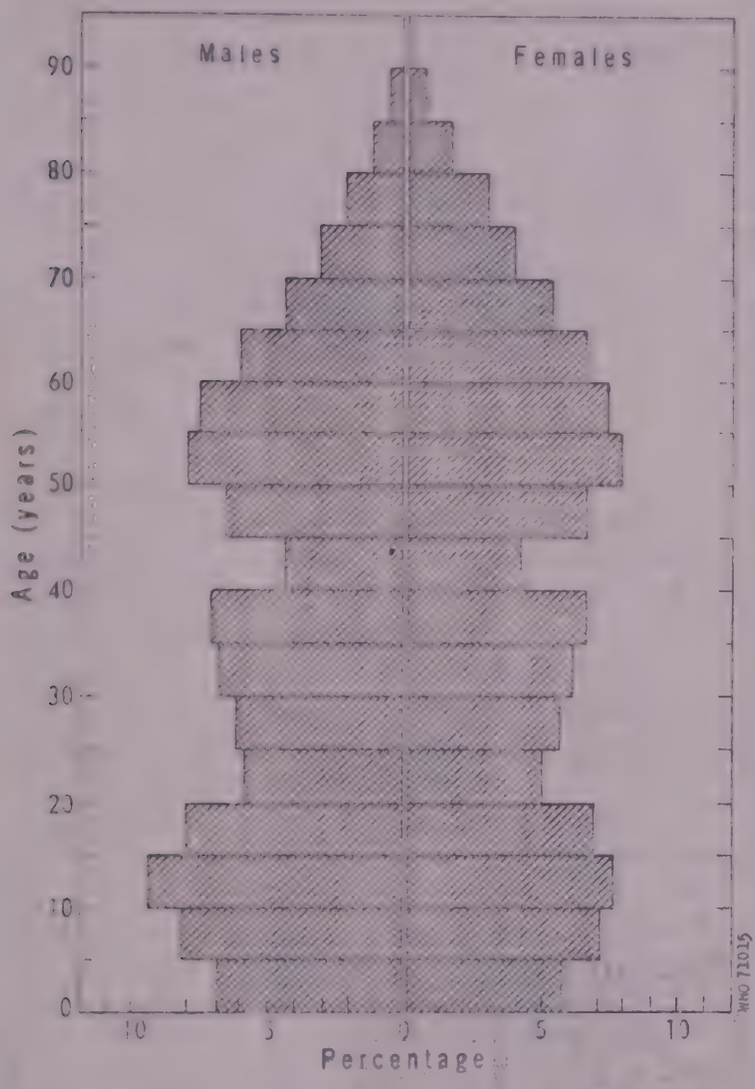
In the course of its first 4 years, the study revealed certain facts which we believe to have a wider application, although we are aware of the necessity to modify some of the methods applied at present. The study has now been in operation for 6 years, and will probably be continued for several more years with a view to obtaining information on long-term trends in the epidemiology of tuberculosis in a given area during the application of appropriate control measures.

DEMOGRAPHIC DETAILS OF KOLÍN DISTRICT

The district of Kolín is situated 50 km to the east of Prague. It covers an area of 829 km², and according to the census taken on 1 March 1961 is inhabited by a total population of 100 418 persons; the population density is thus about 120 inhabitants per km². Children up to the age of 14 make up 22% of the total population, persons aged 15-44 years 36%, those aged 45-64 years 29%, and those over 65 years 13%. Males make up 48% and females 52% of the population (Appendix Table 3, Fig. 3). In 1961 the birth rate was 1.12% and the death rate 1.21% (the absolute number of births was 1126 and that of deaths 1212).

FIG. 3

AGE DISTRIBUTION OF MALE AND FEMALE INHABITANTS OF KOLÍN DISTRICT ON 1 MARCH 1961 [a]



[a] From census data.

As compared with the vital statistics for Czechoslovakia as a whole, with a birth rate of 1.36% and death rate of 0.99%, those for the district of Kolín reveal an age-distribution pattern somewhat favouring higher age-groups.

The town of Kolín has approximately 23 000 inhabitants; the second largest town in the district, Český Brod, has less than 6000 inhabitants; the remainder of the population is divided among another 161 communities.

The region under study is both industrial and agricultural in character; the following branches of industry are represented: heavy engineering, machine-tool and chemical industries, cabinet-making, paper, textile and printing industries. The agricultural workers are either members of farming co-operatives or employees of State farms.

Epidemiological indices for tuberculosis before the commencement of the study did not differ materially from those for the Czech regions in general. The estimated mean incidence of respiratory tuberculosis for the period 1955-59 for Kolín district was 151.8 per 100 000 inhabitants, and for Bohemia and Moravia for the same period 151.7 per 100 000 inhabitants. The mortality, relapse rate and prevalence of active tuberculosis in the district of Kolín were also substantially the same as the national averages. The standard of health service and the facilities available for tuberculosis control likewise corresponded approximately to those prevailing in the other districts of Czechoslovakia.

More detailed information on the epidemiological situation in the district of Kolín at the beginning of study is given in section II under "Results".

II. EPIDEMIOLOGY OF TUBERCULOSIS UNDER THE CONDITIONS OF A NORMAL CONTROL PROGRAMME

METHODS

Tuberculin testing

Tuberculin testing was performed by the intradermal Mantoux test with a dosage of 0.04 μg (2 TU) of PPD 23 in 0.1 ml of a diluent containing Tween 80, produced by the Statens Seruminstitut, Copenhagen. The local reaction was read after 3 to 4 days; the maximum transverse diameter of the induration in millimetres was recorded according to WHO standard procedures. The worker reading the tuberculin tests had no access to information regarding the results of photofluorographic investigations.

Tuberculin testing was carried out on all persons over 6 years of age; schoolchildren were tested at school, persons 15 years of age and over in conjunction with the mass X-ray investigation. In addition, a random sample of 20% of the 3-year-old and 5-year-old children were investigated simultaneously by the intradermal Mantoux test and the tuberculin patch test (Monrad).

BCG vaccination

BCG vaccination was performed in all newborn infants by two intradermal injections, each of 0.1 ml

of BCG vaccine at a concentration of 0.5 mg/ml, without preceding tuberculin tests.

BCG revaccination by intradermal injection of 0.1 ml vaccine at a concentration of 0.75 mg/ml was performed on all persons with tuberculin reactions of up to 5 mm, in all persons of 15 and 19 years of age, and in all persons aged up to 30 years living in contact with tuberculosis patients. In addition, half the number of persons with tuberculin reaction less than 6 mm aged 6 years, 10 years, and over 40 years, selected at random, were vaccinated or revaccinated; the control group received an injection of an equal dose of physiological saline.

Photofluorography

An individual invitation card was sent to each person 15 years of age and over to attend for photofluorographic investigation. The local authorities were responsible for the compilation of the list of inhabitants eligible for investigation, and for the completion and posting of the invitation cards. Individual cards for the registration of the results of the mass investigation were made out later on the basis of the same list of inhabitants.

Those persons not attending for investigation on the first summons received a second, or even a third summons to attend.

The survey was carried out with 2 X-ray units, one mobile and one transportable, fitted with Odelca cameras. Altogether 20 photofluorography centres were established. Persons living more than 2 km away from one of these centres were transported there by buses rented from the Czechoslovak Motor Transport Service.

A 70 mm × 70 mm chest film in the posterior-anterior position was made for each person examined. The X-ray films were developed at a single centre the following morning and independently evaluated by two physicians, who had no information whatsoever regarding the person investigated. When these two disagreed, the film was evaluated by a third physician (arbiter), who knew the results of the evaluation by both readers but no other information; his decision was final.

Photofluorograms were evaluated according to a 3-digit code giving the type of lesion (first digit), its localization (second digit) and size (third digit); see Annex 1.

After evaluation the film was cut up into single films, each of which was then inserted into an envelope bearing the name, date of birth and address of the person investigated. The envelopes containing the films were sent, together with cards giving the results of the photofluorographic evaluation, on the fourth day to the tuberculosis department of the polyclinic concerned together with the daily report on the photofluorographic investigation. This report gave the number of persons investigated and results of investigations, persons with photofluorographic results coded 5-8 (first digit) being listed by name. Such persons were submitted to further investigation at the tuberculosis department of the polyclinic concerned; a standard chest film was made, and supplemented by tomograms if this was considered necessary by the examining physician. Bacteriological investigations were also carried out, and a case-history taken.

Persons with technically inadequate photofluorograms were summoned for a repeat investigation.

In a randomly selected 10% sample of immobile persons not fit to be moved for investigation in 1961, a 35 cm × 35 cm chest film was made with a portable X-ray apparatus at home in bed; in a further 25% sample of immobile persons, material for bacteriological investigation was collected at home.

Hospitalized persons were investigated at the hospital; their full-size films were evaluated by a procedure similar to that for photofluorograms.

Initial bacteriological investigation

An initial bacteriological investigation for tubercle bacilli was carried out for persons registered at the tuberculosis department of the polyclinic as suffering from active or inactive tuberculosis; for persons registered in group P IV (fibrotic lesions in the lungs; see Annex 3); for persons whose photofluorograms had been coded 5-8 (first digit); and, finally, for persons attending the clinic on account of specific symptoms.

The examination consisted of direct microscopy of sputum and culture of sputum and laryngeal swabs. In persons having no sputum the examination was reduced to culture of laryngeal swabs alone.

Persons already on the register, who had been submitted to bacteriological examination before the commencement of the study, were examined on a single day only. Cases with active or suspected active tuberculosis not previously examined bacteriologically had three examinations, on successive days; persons whose photofluorogram had been coded 5-8 (first digit) had one examination only.

In addition, in 1961 bacteriological investigations were carried out on:

(*a*) a 2% random sample of persons with photofluorograms coded 0-3, in order to detect typical or atypical mycobacteria in the population with chest films interpreted as normal;

(*b*) a 10% sample of persons with calcifications (photofluorograms coded 4);

(*c*) a 25% sample of immobile persons not investigated by photofluorography.

Material was collected for bacteriological investigation from persons belonging to the 3 above-mentioned groups on a single day only.

Acid-fast bacilli isolated by the examinations mentioned above were differentiated and investigated for drug-resistance (see Annex 2).

Radiographic and bacteriological follow-up

The frequency of radiographic investigations during the course of treatment and periodical follow-up of persons registered at the tuberculosis department of a polyclinic for active or inactive pulmonary tuberculosis or fibrotic lesions in the lungs varied according to the allocation of persons to individual study groups.

Bacteriological investigations during the operation of the study were carried out according to the techniques employed at the commencement of the study; the material for investigation was collected in a single day.

The frequency of radiographic and bacteriological investigation of persons allocated to the different study groups is shown in Table 1.

The frequency of radiographic and bacteriological investigation of persons with extrapulmonary tuberculosis was determined by the activity of the lesion; in persons with active tuberculosis receiving treatment this investigation was carried out at least twice yearly, in the remaining persons with active tuberculosis once a year.

In all persons registered solely for extrapulmonary tuberculosis a photofluorogram of the chest was obtained annually. Persons with concurrent pulmonary tuberculosis were given the usual radiographic and bacteriological investigation as detailed in Table 1.

Investigation of contacts

This was carried out mainly in the homes of persons excreting *Mycobacterium tuberculosis*, and further in the homes of children and adolescents who displayed a significantly high-intensity tuberculin reaction, in a random sample of older individuals with a high-intensity tuberculin reaction, on farms and in other places of work with occupational contact with animal sources of *Myco. tuberculosis* var. *bovis*.

Basic investigations in the homes under study were performed by an epidemiologist or by fully trained auxiliary medical personnel.

Further epidemiological investigations, where necessary, were carried out in collaboration with the public health service or in some cases the veterinary and sanitary service.

Extrapulmonary tuberculosis

Case finding for extrapulmonary tuberculosis was not conducted on such a wide scale as was that for

TABLE 1

FREQUENCY OF RADIOGRAPHIC AND BACTERIOLOGICAL INVESTIGATIONS

	Bacteriological investigation	Radiographic investigation
Active tuberculosis		
Institutional treatment	Every month	On admission to and discharge from hospital. During hospital stay every 3 months on an average
Ambulatory treatment with antituberculosis drugs	Every 3 months	Once every 6 months and at termination of therapy
Follow-up	Every 6 months	Once a year
Inactive tuberculosis		
Follow-up	Every 6 months	Once a year, by photofluorography
Fibrotic lesions in lungs		
Follow-up	Once a year	Once a year, by photofluorography

pulmonary tuberculosis; as a general rule only persons who sought medical care from the appropriate specialists on account of clinical symptoms due to tuberculosis were registered as having extrapulmonary tuberculosis. The registration, epidemiological investigation and recording procedures for persons registered as having extrapulmonary tuberculosis did not differ from those employed for persons suffering from pulmonary tuberculosis.

Recording and reporting procedures

Recording. Two main cards were used for recording the results of the study. One card was completed for all persons aged 6 years and over. It contains basic information such as personal data of the examinee, the results of the evaluation of the tuberculin test, the interpretation of the photofluorogram by both readers, the arbiter's decision if required, the disease group to which the person was allocated (see Annex 3), and data on BCG vaccination if applicable.

The other card was completed for all persons registered as suffering from active or inactive tuberculosis or fibrotic lesions in the lungs and contained basic information on the person registered and the course of the disease.

In addition, separate cards were used for cases where investigations were carried out at the focus of infection, and for persons excreting *Myco. tuberculosis* var. *hominis* or var. *bovis*.

Reporting. All newly notified cases, relapses and chronic bacillary excretors were reported to the Ministry of Health (*via* the Regional Officer for Tuberculosis). These terms are explained below.

(1) A *newly notified case* of tuberculosis is a case of active tuberculosis discovered in the calendar year in question in a person never before registered as having tuberculosis.

If the patient was reported in the same calendar year as having both pulmonary and extrapulmonary tuberculosis, the case was registered as a new case of pulmonary tuberculosis.

(2) The finding of tubercle bacilli and/or radiographic progression of the tuberculous lesion in persons registered in the inactive tuberculosis group during the course of a given calendar year was considered as evidence of *relapse*.

(3) A patient who was assigned to the bacillary tuberculosis group more than 2 years previously and remained in this group without interruption up to the day of evaluation was classified as a *chronic bacillary excretor*. Only in those cases where all bacteriological investigation results had been negative during the past 12 months was a patient transferred from the bacillary tuberculosis group to the bacteriologically quiescent tuberculosis group.

Classification of disease

Cases with pulmonary and extrapulmonary tuberculosis on the files of the tuberculosis department of the polyclinics concerned at the start of the study and cases notified during the study were classified according to the scheme shown in Table 2.

Persons with active pulmonary tuberculosis found (by microscopy, culture or animal experiment) to be excreting tubercle bacilli in the sputum on at least one occasion during the past 12 months were classed as having bacillary tuberculosis (group P I-A). After no signs of tubercle bacilli had been found in the sputum for 12 months, these persons were transferred to the subgroup " bacteriologically quiescent tuberculosis " (P II-A), where they remained either 1 or 2 years, depending on whether cavitation was absent or present at the time their active tuberculosis was detected. Persons with newly detected active tuberculosis in whom excretion of mycobacteria could not be demonstrated were assigned to the subgroup " active non-bacillary tuberculosis " (P I-B) and remained there for 2 years.

All persons previously registered as having bacteriologically quiescent tuberculosis or active non-bacillary tuberculosis were registered as having inactive tuberculosis on leaving these groups; they remained registered in this group for the rest of their lives. In this group, persons with lesions whose tuberculous etiology had previously been confirmed bacteriologically or histologically were listed separately (P III-A) from those where the diagnosis of active tuberculosis had been established solely from radiological investigation and lacked bacteriological confirmation (P III-B).

Persons suffering from extrapulmonary tuberculosis were classified on lines similar to those for persons with pulmonary tuberculosis.

Persons with photofluorograms showing fibrotic lung lesions but without evidence of disease activity were registered in group P IV.

Further details on the classification of pulmonary and extrapulmonary tuberculosis as used in this study are given in Annex 3.

Prevalence and incidence

In order to avoid possible misunderstandings, it is perhaps as well to give here the definitions of

TABLE 2

CLASSIFICATION OF CASES OF PULMONARY TUBERCULOSIS

	Tuberculosis bacteriologically confirmed	Tuberculosis not bacteriologically confirmed
Active tuberculosis	P I-A: *Bacillary tuberculosis* (Persons remain registered for 12 months after reversal of infection)	P I-B: *Active non-bacillary tuberculosis* (Persons remain registered for 24 months after reversal of infection)
	P II-A: *Bacteriologically quiescent tuberculosis* (Persons remain registered for 12 months after reversal of infection if no cavitation was present when the active tuberculosis was detected and 24 months if cavitation was present)	
Inactive tuberculosis	P III-A: *Inactive tuberculosis previously bacteriologically or histologically confirmed* (Persons registered permanently)	P III-B: *Inactive tuberculosis not previously bacteriologically or histologically confirmed* (Persons registered permanently)
Fibrotic lesions in lungs	P IV: *Fibrotic lung lesions* (Persons registered permanently)	

prevalence and incidence used in this study. The (*point*) *prevalence* is the number of persons with a given condition on a given date (31 December of the year in question). Thus, the prevalence of newly notified cases of tuberculosis is the number of persons in the district on 31 December of a given year who within that calendar year had been notified for the first time as having tuberculosis; it does not include persons who had died during the year or had moved from the district, but it does include persons who had moved to the district since they had been registered as having tuberculosis. The *incidence*, on the other hand, is the number of persons registered as having the condition in question between 1 January and 31 December: it does include persons who died or moved from the district during the year, and it does not include persons who moved to the district after being registered as having the condition. This difference should be borne in mind when comparing the data given in this paper.

RESULTS

Tuberculin testing and BCG vaccination

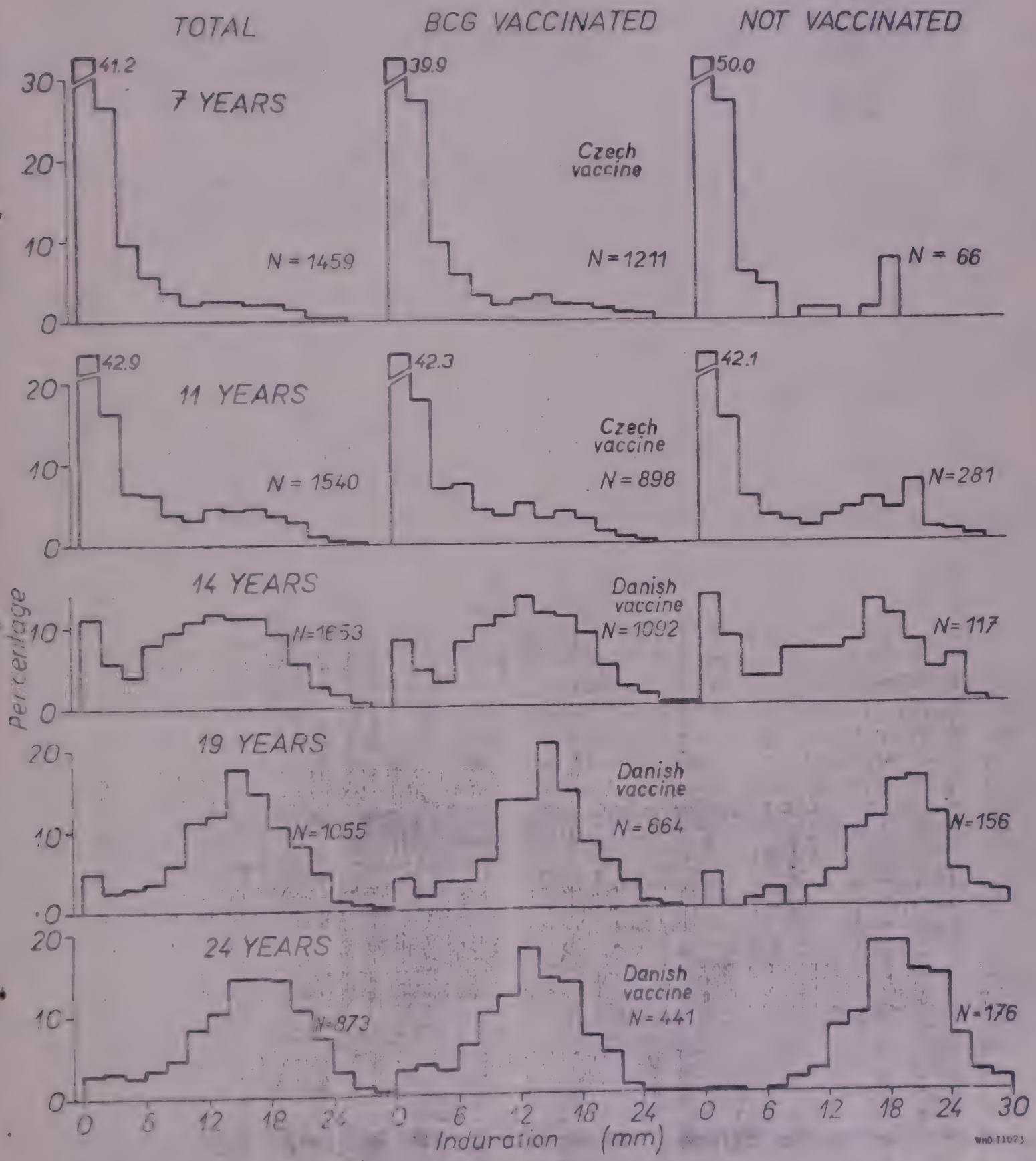
Tuberculin tests were carried out in 1961 on 88.7% of the male inhabitants of the district of Kolín eligible for investigation, and on 91.0% of the eligible female inhabitants. Full details of the distribution of tests according to age and sex are given in Appendix Table 4. The results of the tests are summarized in Fig. 4 and Fig. 5. (Full details are given in Appendix Tables 5 and 6.)

The effect of vaccination on the tuberculin reaction. Fig. 4 shows the distribution of the intensity of the tuberculin reaction for vaccinated and unvaccinated persons of selected ages between 7 and 24 years. The unvaccinated group was much smaller, in view of the high vaccination coverage of the age-groups in question, but it will be seen that vaccination does tend to reduce the intensity of the positive tuberculin reactions from about 18 mm on the average to about 14 mm on the average. A very considerable increase in "positive" reactions with age was also found: for example, for the vaccinated subjects the percentage with indurations of diameter 5 mm or less fell from 77.1% at age 7 years to 9.8% at age 24 years, while the percentage with indurations of diameter 12 mm or more rose from 11.9% at 7 years to 70.7% at 24 years, as may be seen from Table 3.

The effect of time, age and diagnosis on the tuberculin reactions. In a proportion of the population,

FIG. 4

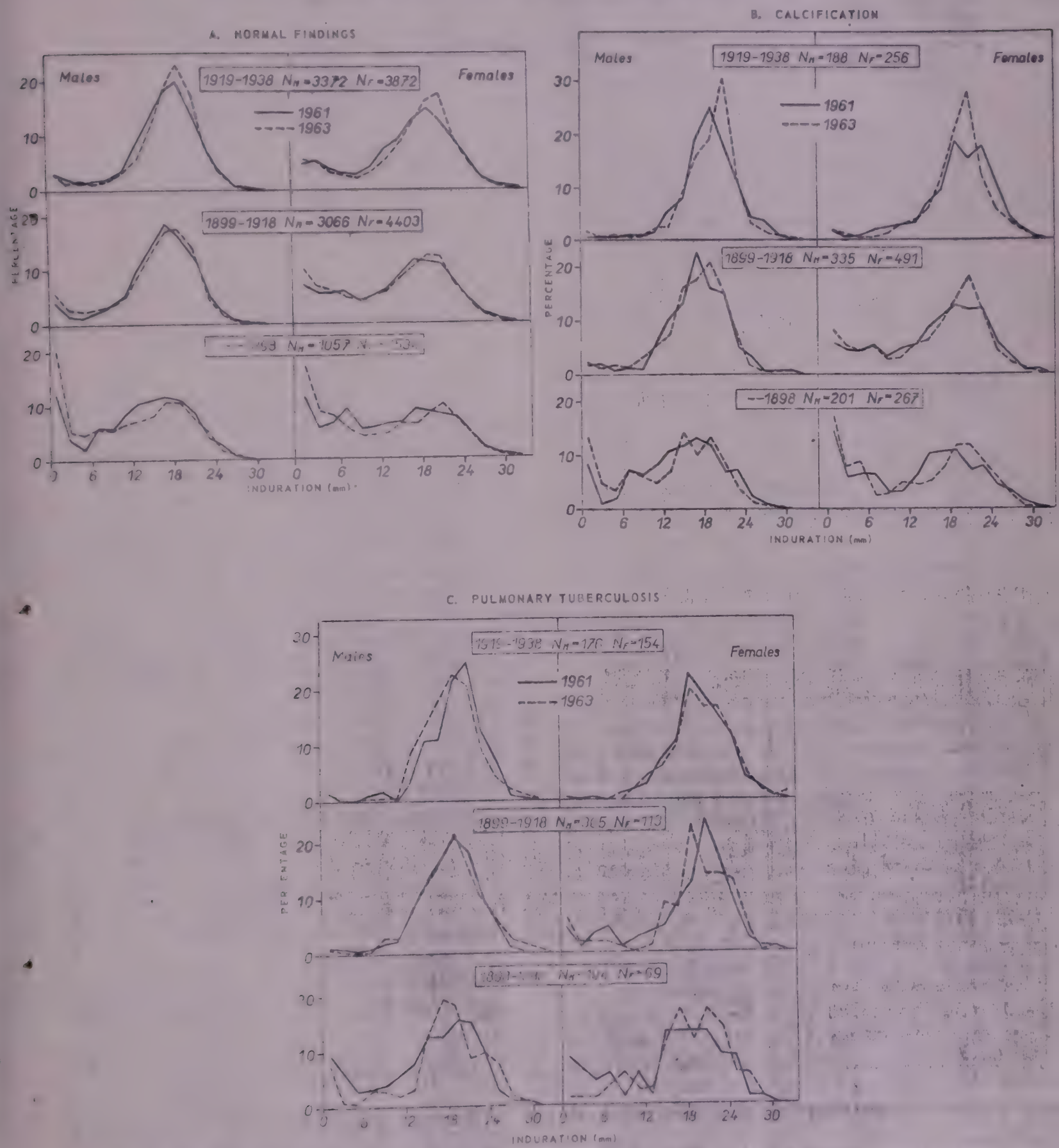
SIZE DISTRIBUTION OF TUBERCULIN REACTIONS IN KOLÍN DISTRICT IN 1961, BY AGE AND VACCINATION STATUS[a]



[a] Tuberculin testing was carried out with 2 TU of PPD 23 in Tween 80. The number of persons tested, N, is given above each histogram.

FIG. 5

SIZE DISTRIBUTION OF TUBERCULIN REACTIONS IN KOLÍN DISTRICT IN 1961 AND 1963, BY AGE, SEX AND PHOTOFLUOROGRAPHIC STATUS[a]



[a] Tuberculin testing was carried out with 2 TU of PPD RT 23 in Tween 80. The years of birth of the persons involved and the number of males, NM, and of females, NF, tested are given above each graph.

TABLE 3

DISTRIBUTION OF TUBERCULIN REACTIONS IN BCG-VACCINATED SUBJECTS AGED 7, 11, 14, 19 AND 24 YEARS IN KOLÍN DISTRICT [a]

Age (years)	No. of persons examined	Percentage of subjects with diameter of induration (mm)				BCG vaccine produced in
		0-5	6-11	12-17	18+	
7	1 211	77.1	11.0	7.7	4.2	Czechoslovakia
11	898	67.0	15.0	12.0	6.0	Czechoslovakia
14	1 092	15.7	29.0	36.1	19.2	Denmark
19	664	9.2	23.0	48.5	19.3	Denmark
24	441	9.8	19.5	43.8	26.9	Denmark

[a] Tuberculin testing was carried out by the Mantoux intradermal test using 2 TU of PPD RT 23 in Tween 80.

the tuberculin test was repeated in 1963. Fig. 5 shows the distribution of the intensity of the tuberculin tests in both years for persons (aged 23 years or more in 1961) with normal fluorograms (Fig. 5A), with fluorograms showing evidence of calcification in the lungs, hilum nodes, or both (Fig. 5B) and with bacteriologically confirmed tuberculosis (Fig. 5C). It will be seen that there is no appreciable change in the distribution either with time between 1961 and 1963, with the age of the subjects, or with the diagnosis. We saw above that there was a definite increase in the intensity of the reaction with age from the age of 7 years to 24 years; this increase would seem to have reached "saturation" by the age of 24 years. Indeed, it may be seen from Appendix Table 6 A that the estimated percentage of positive reactions (estimated by the method of the normal truncated distribution, with the point of truncation at 12 mm) actually falls off by 10%–20% as the age of the subjects rises from 25 years–44 years to 65 years or above; this, however, is probably due to a reduction in the sensitivity of the skin with ageing rather than to a reduction in tuberculosis infection.

Prevalence of active pulmonary tuberculosis

Over-all trends. The prevalence of active tuberculosis as of 31 December of each year for the years 1960-64 is given in Table 4 (for full details see Appendix Table 7).

We will confine ourselves here to a discussion of the values for bacillary tuberculosis, since it represents the most important source of the human type of tubercle bacilli in the community. The other forms of active tuberculosis in man have only secondary interest, and, moreover, show trends similar to those of bacillary tuberculosis.

The bacillary tuberculosis group may be divided into the following four subgroups:

(*a*) newly discovered bacillary pulmonary tuberculosis,

(*b*) tuberculosis relapses confirmed bacteriologically,

(*c*) chronic bacillary excretors,

(*d*) remaining cases.

Persons with bacteriologically confirmed tuberculosis found during the year in question, and not previously notified as having active disease, were assigned to subgroup (*a*). The finding of tubercle bacilli in persons registered as having inactive tuberculosis was regarded as evidence of relapse,

TABLE 4

PREVALENCE RATE (PER 100 000) OF ACTIVE PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, BY TYPE OF DISEASE

Year	Prevalence rate (per 100 000)			
	P I-A	P II-A	P I-B	Total
1960	150	172	99	421
1961	233	129	92	454
1962	138	199	80	417
1963	126	181	45	352
1964	91	126	45	262

TABLE 5

PREVALENCE RATE (PER 100 000) OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, BY TYPE OF DISEASE [a]

	Prevalence rate (per 100 000)				
	1960	1961	1962	1963	1964
Newly discovered cases	46 (21)	132 (27)	61 (24)	88 (26)	47 (18)
Relapses	29 (10)	25 (8)	18 (9)	13 (5)	16 (5)
Chronic bacillary excretors	49 (42)	40 (19)	17 (6)	11 (6)	8 (5)
Remainder	26 (7)	36 (14)	42 (11)	14 (6)	20 (6)
Total	150 (80)	233 (88)	138 (50)	126 (43)	91 (34)

[a] The number of cases found by direct smear microscopy is given in parentheses.

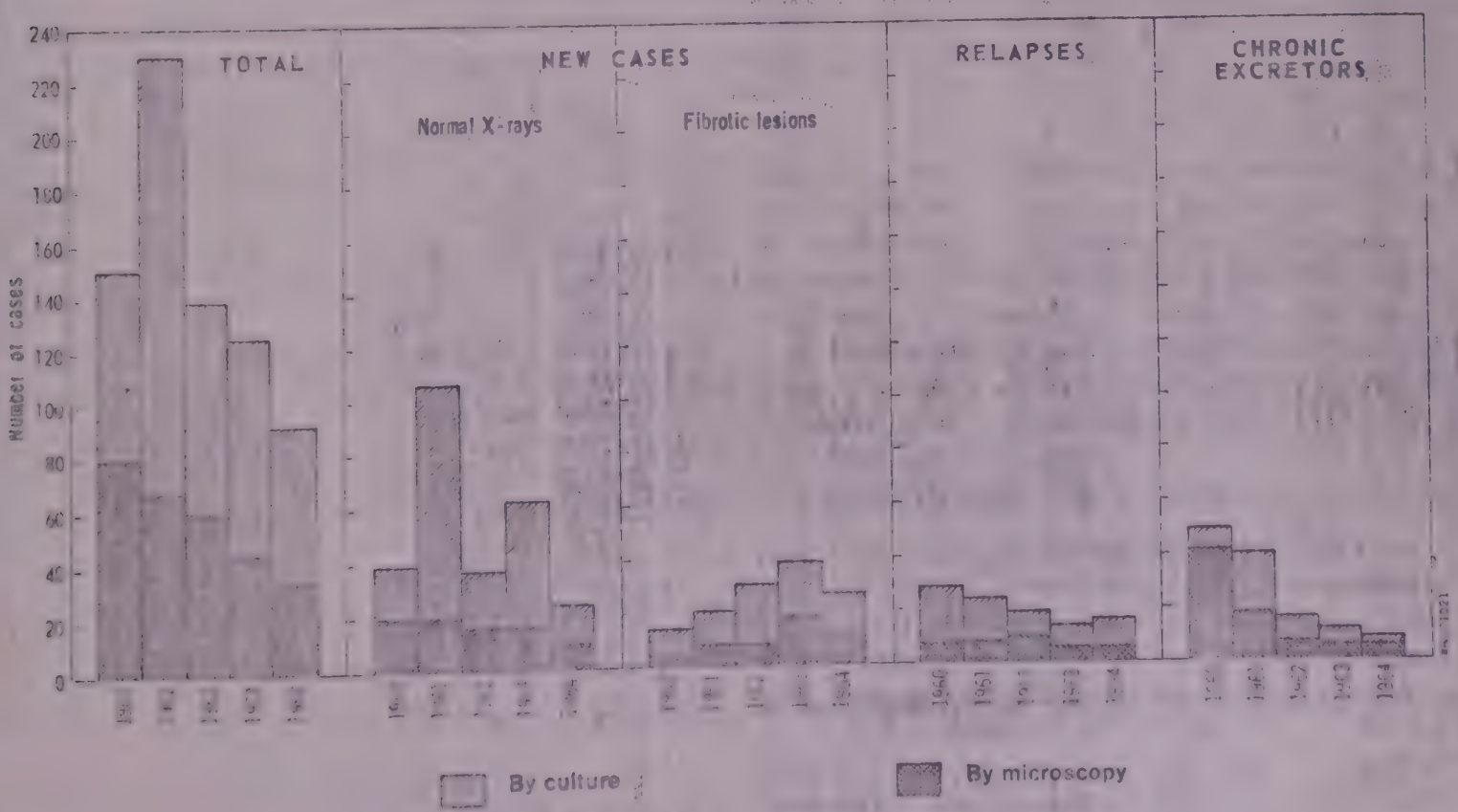
and such persons were allotted to subgroup (*b*). Persons who had persistently excreted tubercle bacilli during the previous two years, or even longer, were assigned to subgroup (*c*). All those who could not be allotted to any of the first three subgroups, particularly persons who had been registered the previous year as having newly discovered tuberculosis or a relapse and who were found to have excreted tubercle bacilli at least once again during the year studied, were placed in subgroup (*d*).

The prevalence of bacillary pulmonary tuberculosis during the years 1960-64, classified as described above, is given in Table 5 (for full details, see Appendix Table 8).

Table 5 and Fig. 6 show that the prevalence of bacillary tuberculosis increased appreciably from

FIG. 6

PREVALENCE OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, WITH BREAKDOWN BY TYPE OF DISEASE



1960 to 1961, as a result of the mass examination carried out in the latter year. In 1962 there was a considerable decrease in prevalence. This decrease continued, though less steeply, in 1963—even though a second mass photofluorographic examination of the population over 15 years of age was made in that year—and in 1964. The total number of persons with bacillary tuberculosis decreased from 150 in 1960 to 91 in 1964 (i.e., by 39%).

The trends in the number of newly discovered cases will be discussed below, under "Incidence", and those in the number of relapses under "Relapses".

Table 5 further reveals that the total number of persons in whom tubercle bacilli were found by direct smear microscopy decreased from 80 in 1960 to 34 in 1964 (by 57%), although the mass photofluorographic examinations of 1961 and 1963 resulted in a marked increase in the total number of persons with known bacillary tuberculosis. It is interesting to note that the number of new cases—confirmed by the demonstration, by direct microscopy, of tubercle bacilli in the sputum—did not differ greatly from one year to another during the period 1960-64, and was not substantially influenced by the photofluorographic examinations; for the successive years in question the figures were 21, 27, 24, 26 and 18 patients per 100 000 inhabitants.

The decrease in the total prevalence of bacillary tuberculosis detected by direct smear microscopy in the years 1960-64 was caused mainly by a drop in the numbers of chronic bacillary excretors (from 49 in 1960 to 8 in 1964). This drop is a reflection of the success of the chemotherapy used, and is discussed further in the section on the epidemiologi impact of mass treatment.

The improvement in the prevalence of bacill tuberculosis was accompanied by a decrease in t severity of the disease, as shown in Table 6. It w be seen that, for example, the proportion of advanced cases of bacillary tuberculosis fell by h between 1960 and 1964 (from 41% to 20%); t absolute decrease in the number of advanced ca was even more marked (from 61 to 18). A simi trend was observed for cavitation as found tomography; the number of cases with cavitati of the lungs fell from 99 (66%) in 1960 to 34 (37 in 1964.

Influence of sex and age. At the start of the stu the highest number of cases of bacillary tuberculo was registered in males over 45 years of age, wit maximum of 480 per 100 000 at ages from 45 years 64 years; the prevalence in women was relatively l in all age-groups, and did not rise above 105 100 000 (Appendix Table 7 and Fig. 7). After the f mass investigation of the population in 1961 there w an increase in the number of males registered as h ing bacillary tuberculosis in middle and old age; men between 45 years and 64 years the prevale was 634 per 100 000, and in men over 65 ye 773 per 100 000. There was an insignificant crease in the prevalence of bacillary tubercul amongst women younger than 65 years, but in over-65 age-group there was a very large incre to 383 per 100 000. In the further years of the st the age distribution of bacillary tuberculosis in m shifted to higher age-groups, while in both se the absolute prevalences declined markedly, pe

TABLE 6

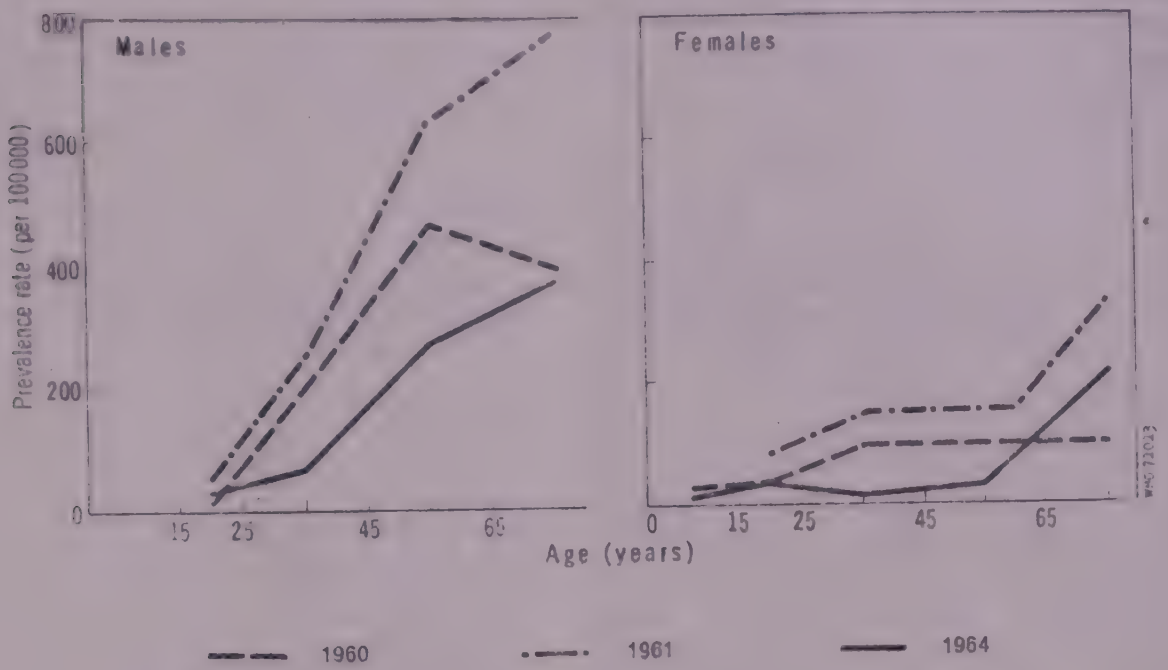
EXTENT OF DISEASE IN PERSONS REGISTERED FOR ACTIVE TUBERCULOSIS IN KOLÍN DISTRICT IN 1960 AND 1964 [a]

Extent of disease	Bacillary tuberculosis (P I-A)				Bacteriologically quiescent tuberculosis (P II) and active non-bacillary tuberculosis (P I-B)			
	1960		1964		1960		1964	
	No.	%	No.	%	No.	%	No.	%
Minimal	21	14	33	36	129	47	105	61
Moderately advanced	68	45	40	44	116	43	56	33
Far advanced	61	41	18	20	26	10	10	6
Total	150 (99)	100 (66)	91 (34)	100 (37)	271 (41)	100 (15)	171 (23)	100

[a] The total number of cases with cavitation is shown in parentheses.

FIG. 7

PREVALENCE RATE (PER 100 000) OF BACILLARY PULMONARY TUBERCULOSIS IN KOLIN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, BY SEX AND AGE



cularly in young and middle-aged persons; in 1960 there were 24 men and 16 women up to 44 years of age with bacillary tuberculosis, in 1964 only 11 men and 4 women.

Prevalence of inactive pulmonary tuberculosis

The prevalence of inactive pulmonary tuberculosis at the start of the study was 1147 and increased steadily throughout the study, reaching 1533 in 1964 (an increase of 34%). This is shown in Table 7 (full details are given in Appendix Table 7).

Since the group of inactive pulmonary tuberculosis is formed by persons who were previously in the active group and for whom there is no longer any evidence of active disease, this increase in the prevalence of inactive pulmonary tuberculosis may be regarded as a further reflection of the success of the control programme.

TABLE 7

PREVALENCE RATE (PER 100 000) OF INACTIVE PULMONARY TUBERCULOSIS IN KOLIN DISTRICT IN 1960–64

Year	Prevalence rate (per 100 000)	Previously bacteriologically (or histologically) confirmed	
		No.	%
1960	1 147	666	58
1961	1 258	734	58
1962	1 325	792	60
1963	1 448	867	60
1964	1 533	963	63

The prevalence of inactive pulmonary tuberculosis was 1.3 times higher in men than in women, both in 1960 and in 1964.

The distribution of inactive tuberculosis according to age remained practically the same for women in all 4 years of the study, with the highest incidence in the age-group 25 years–44 years (1854 per 100 000 in 1960 and 2227 per 100 000 in 1964). In men there was an increase in the number of persons registered in the age-groups over 45 years, particularly in the age-group of 65 years and over (from 1798 per 100 000 in 1960 to 3412 per 100 000 in 1964).

Incidence of pulmonary tuberculosis

Over-all trends. In 1961-64 active pulmonary tuberculosis was detected for the first time in 473 persons. Moreover, at necropsy of about one-third of all persons who died in the Kolín district tuberculosis was found in another 21 individuals who had not been registered as having tuberculosis.

Bacteriological proof of tuberculosis was obtained in 348 cases (74%); in 125 cases (26%) the diagnosis was established solely on radiographic evidence

(Appendix Table 9). In this section we will only deal with the incidence of bacillary tuberculosis.

New bacillary cases were discovered both among persons with previously normal chest X-rays and among persons registered as having fibrotic lung lesions. The first group yielded a total of 241 bacillary cases during the 4-year period, and the second 107, as may be seen in Table 8 (for full details see Appendix Table 10).

The greatest number of new bacillary tuberculosis cases was found in 1961, the year of the first mass photofluorographic investigation of the population over the age of 14 years. The second mass investigation carried out in 1963 yielded less than half as many new cases of bacillary tuberculosis as in 1961. In 1962 and 1964, new cases were discovered mainly among persons with previously negative chest X-rays who consulted a physician on account of symptoms, and in persons registered as having fibrotic lung lesions. A total of 66 persons were investigated on account of symptoms during the 4-year period, 16 or 17 per year. In the group of patients whose tuberculosis was discovered by photofluorography, 59 persons out of 148 (40%) complained of subjective symptoms at the time of diagnosis, but had not sought medical advice; bacillary tuberculosis ran an asymptomatic course at the time of investigation in the remaining 89. The number of new cases of bacillary tuberculosis in the group of persons registered for fibrotic lung lesions depended on the discrepancy between the registered prevalence of fibrotic lesions and the true state of affairs; for this reason their number rose following the first mass photofluorographic investigation.

Mycobacteria were found by microscopy of direct smears in 102 (29%) persons with bacillary tuberculosis. Patients found to be suffering from bacillary tuberculosis by investigation done on account of subjective symptoms had mycobacteria found by microscopic examination in 38% of the cases, persons whose disease was detected by photofluorography in only 16% (Appendix Table 10). The number of such cases per year remained practically unchanged from 1961 to 1964, being 27 in 1961 and 20 in 1964 (Appendix Table 10). In a certain number of persons, the disease advanced during a few months ("rapid cases"). These progressive lesions, frequently with tubercle bacilli found by direct microscopy, affected middle-aged and elderly persons. Bacillary tuberculosis in these persons was frequently accompanied by symptoms.

It should be noted that in 1964 the number of persons with cavitary tuberculosis was only 17 as compared with 48 in 1961 (Fig. 8).

The effect of age and sex. The age distribution of new cases of bacillary tuberculosis is shown separately for males and females in Appendix Table 9 and Fig. 9. In males, the incidence rose fairly uniformly with age up to the highest age-group. As regards women, relatively few cases of bacillary tuberculosis were found up to the age of 64 years, relatively most cases at ages over 65 years. The form of the age distributions for both sexes did not change appreciably throughout the period of the study, though, of course, values were lower in 1963 and 1964 than in the first two years.

Accuracy of the incidence estimates. The number of newly discovered cases of tuberculosis for the years 1961-64 is not equal to the true incidence of tuberculosis during this period, as it was increased by cases which had originated before the start of the study and were discovered during its operation, and reduced by asymptomatic cases which originated after the second photofluorographic investigation of the population and escaped detection in 1964.

In order to gain an idea of the difference between the number of cases of bacillary tuberculosis discovered and its true incidence, we carried out—as already mentioned—two photofluorographic investigations of the inhabitants over 14 years of age

TABLE 8

NEWLY NOTIFIED CASES OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY MODE OF DETECTION [a]

Mode of detection	No. of cases				
	1961	1962	1963	1964	Total
Previously normal chest X-rays					
On account of symptoms	17	16	16	17	66
By mass photofluorography	97	10	41	—	148
By other preventive examination	5	11	4	7	27
Total	119	37	61	24	241
Previous fibrotic lung lesions					
All methods	19	29	34	25	107
Grand total	138	66	95	49	348

[a] The data given in this table are all for living persons. In addition, 5 previously unknown cases of bacillary pulmonary tuberculosis were found by post-mortem examination in 1961, 4 in 1962, 8 in 1963 and 4 in 1964—a total of 21.

FIG. 8
NEW CASES OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY BACTERIOLOGICAL AND PHOTOFLUOROGRAPHIC STATUS

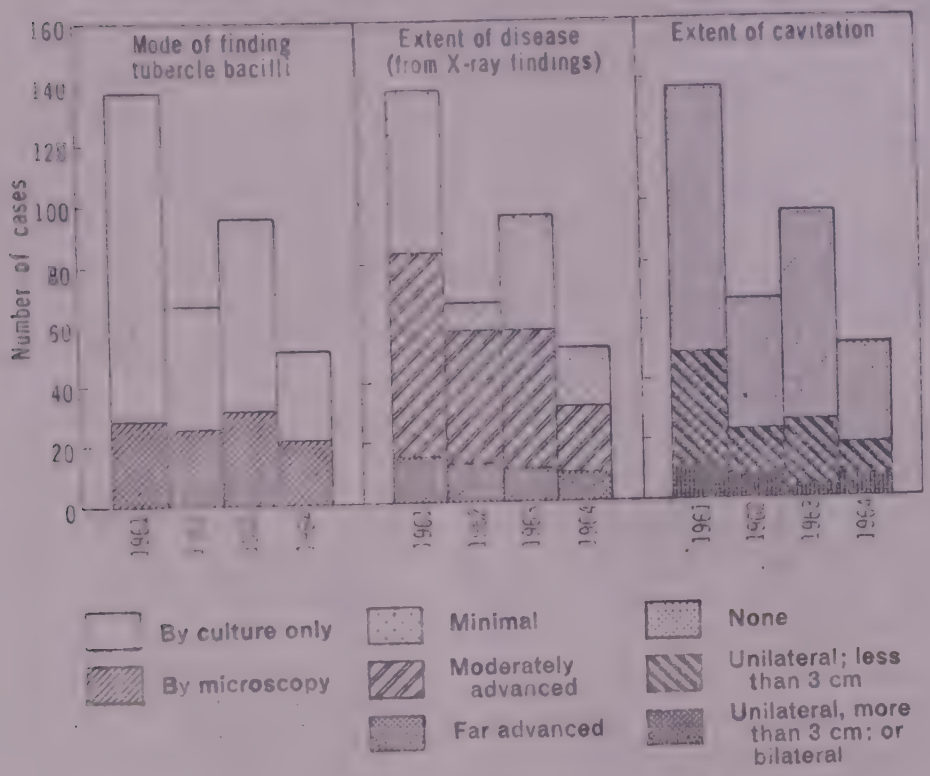
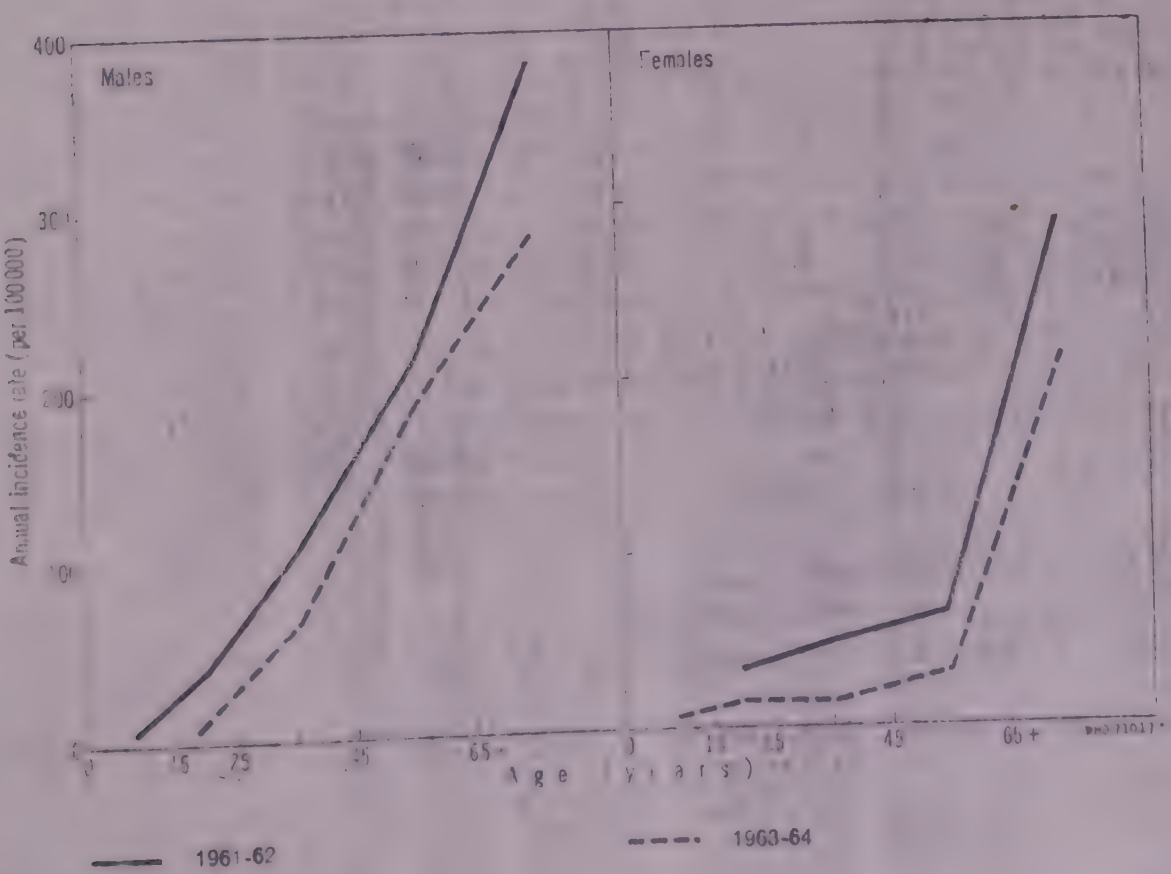


FIG. 9
AVERAGE ANNUAL INCIDENCE RATE (PER 100 000) OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-62 AND 1963-64, BY SEX AND AGE



(in 1961 and 1963). These investigations enabled us to make a sufficiently accurate estimation of the true incidence of bacillary tuberculosis in 1962 and 1963, which amounted to approximately 41 cases per 100 000 inhabitants per year—or 44 cases per year per 100 000 persons with normal photofluorographic findings (Appendix Table 11).

The number of newly diagnosed cases of bacillary tuberculosis in 1961-64 is compared with the estimated true incidence in Appendix Table 12. We assume that under a tuberculosis programme like that maintained in the Kolín district in recent years, the incidence of persons excreting tubercle bacilli falls on the average by 10% annually. If the average annual incidence of bacillary tuberculosis in the Kolín district in 1962 and 1963 was 41 per 100 000 population, the assumption of a 10% annual decrease would mean that the incidence was 43 in 1962 and 39 in 1963, per 100 000 population. The total number of newly diagnosed cases of bacillary tuberculosis in 1961-64 was 76 more than was the estimated incidence. The highest number of newly diagnosed cases was found as a result of mass photofluorographic examination of the population in the first year of the study (1961), when it exceeded the expected incidence by 71. In 1963, when the photofluorographic investigation was repeated, 22 more cases of bacillary tuberculosis were notified than expected; on the other hand, in 1964 there was a deficit of 11.

Relapses

Bacteriological or X-ray evidence of tuberculosis in persons registered as having inactive tuberculosis (groups P III-A, P III-B; Annex 3) was regarded as evidence of relapse.

During the four years of the study, relapses occurred in a total of 91 persons; in 80 of these (88%) it was verified bacteriologically, in the other 11 by photofluoroscopy only (Appendix Table 13). The following section deals only with relapses that were verified bacteriologically.

There were 63 relapses (79%) in males, and 17 (21%) in females. The highest number of relapses was found in the first year of the study, in all probability because the detailed bacteriological investigations disclosed several unknown cases of relapse originating from previous years. In the second, third and fourth years of the study, the number of relapses was lower and ranged between 14 and 20. That no marked decline occurred during this period is probably due to the fact that the therapeutic measures introduced during the course of the study, although adequate, had not had time to take full effect—and also to the fact that the absolute number of persons registered as having inactive tuberculosis increased.

Tubercle bacilli were found by microscopic examination in 30 (38%) of all bacillary cases of relapse; in nearly two-thirds of the cases, bacilli were found in sputum or laryngeal swab cultures (see Table 9).

Relapse was found in 25 persons (31%) during investigations on account of symptoms, and in 55 (69%) during the regular check-up of persons registered for inactive tuberculosis. These proportions did not vary appreciably between patients with positive direct smears and patients positive by culture only. Only 10 patients with relapse verified by microscopical demonstration of mycobacteria in the sputum sought advice of their own accord on account of symptoms. In 20 persons, in spite of massive excretion of tubercle bacilli, relapse was not discovered until the regular check-up.

An indication of the extent of tuberculous lesions in relapse is given not only by the bacteriological findings, but also by the tomographic evidence of cavitation. Cavitary tuberculosis was found in 34

TABLE 9

RELAPSES OF BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY MODE OF DETECTION OF TUBERCLE BACILLI

Mode of detection	1961	1962	1963	1964	Total	
					No.	%
Microscopy (and culture)	11	9	5	5	30	38
Culture only	18	11	9	12	50	62
Total	29	20	14	17	80	100

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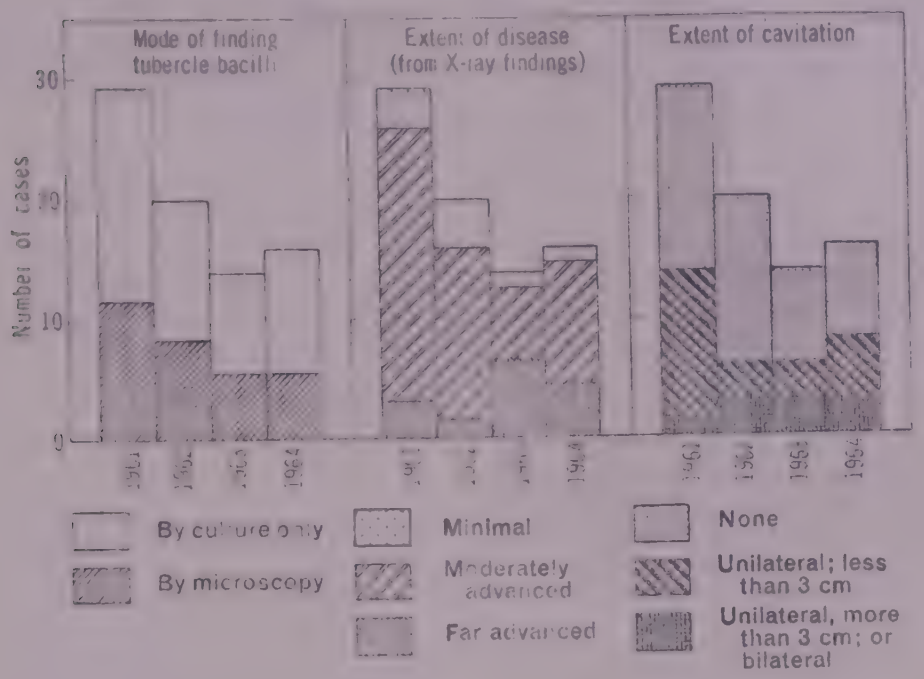
FIG. 10

RELAPSES OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY BACTERIOLOGICAL AND PHOTOFLUOROGRAPHIC STATUS



(43%) relapses, with only random variations from year to year. There was a similar fluctuation in the number of persons with moderately advanced and advanced tuberculosis; in all the years studied, cases of moderately advanced tuberculosis predominated (Fig. 10).

Tuberculosis relapses generally occurred a relatively long time after the last demonstration of mycobacteria. In more than two-thirds (44) of the 58 cases in which the original disease was confirmed bacteriologically, relapse occurred after a lapse of more than 2 years; only in 1 patient were mycobacteria found again in the third year, and in 13 persons in the fourth or fifth year after sputum conversion.

The risk of relapse also depended on whether mycobacteria had been found in the previous active phase, and varied with age and sex. In 1961-64 patients who had previously excreted tubercle bacilli suffered relapse about twice as frequently as persons with inactive tuberculosis never before confirmed bacteriologically; the mean figure for the 4 years was 2.0% annually for the former group, and 0.9% for the latter (Table 10).

TABLE 10

RELAPSES OF BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, IN PERSONS REGISTERED FOR INACTIVE TUBERCULOSIS, BY CLASSIFICATION OF PREVIOUS CONDITION

Disease group	1961		1962		1963		1964		Total	
	No.	% [a]	No.	% [a]	No.	% [a]	No.	% [a]	No.	% [a]
P [illegible]-A	21	3.2	11	1.5	13	1.6	15	1.7	60 [b]	2.0
P [illegible]-B	8	1.7	9	1.7	1	0.2	2	0.3	20	0.9
Total	29	2.5	20	1.6	14	1.0	17	1.2	80	1.6

[a] Percentage of persons registered for inactive tuberculosis.

[b] 58 cases were originally confirmed bacteriologically, and 2 histologically.

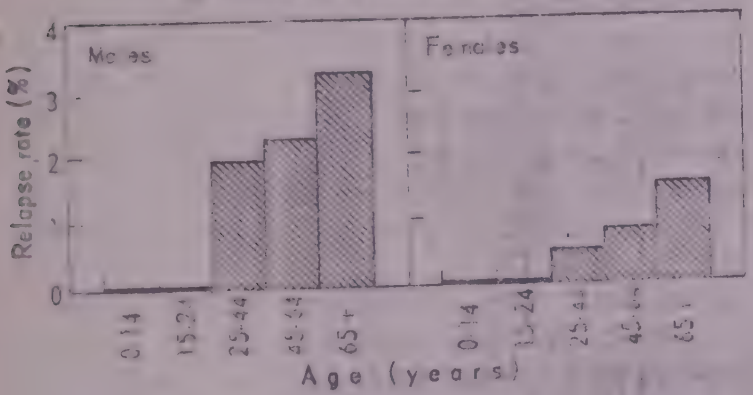
TABLE 1[a]

TUBERCULOSIS MORTALITY IN KOLÍN DISTRICT IN 1961-64

Age-group (years)	1961		1962		1963		1964		Total		
	M	F	M	F	M	F	M	F	M	F	Total
Persons registered for tuberculosis before death											
0-44	—	—	—	—	1	—	—	—	1	—	1
45-70	5	1	4	2	—	—	2	—	11	3	14
71 +	3	2	1	4	3	2	2	—	9	8	17
Total	8	3	5	6	4	2	4	—	21	11	32
Persons not registered for tuberculosis before death											
45-70	1	—	—	—	1	1	—	—	2	1	3
71 +	—	—	—	1	—	—	—	2	—	3	3
Total	1	—	—	1	1	1	—	2	2	4	6
Grand total	9	3	5	7	5	3	4	2	23	15	38

FIG. 11

AVERAGE ANNUAL RELAPSE RATE (%) OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64



The variation of the risk of relapse with age and sex is shown in Fig. 11. Relapse was not found in persons up to 24 years of age of either sex; however, the number of persons registered as having inactive tuberculosis in this age-group was very low. In men older than 25 years, the mean annual relapse rate increased from 1.6 % in persons aged from 25 years to 44 years to 3.2% in those over 65. In women up to 64 years of age, the annual incidence of relapse was lower than 1% and rose to 1.5% annually only in the 65-and-over age-group.

The relatively high number of relapses in the first 4 years of the study may be regarded as being due to the inadequate therapy received by a proportion of the patients with active tuberculosis in past years.

Mortality

Of the permanent residents of the district of Kolín, a total of 38 persons died from tuberculosis of all types in the period 1961-64; 6 of these had not been registered as having tuberculosis before their death. Table 11 lists the number of deaths in the individual years according to age and sex.

It may be seen that death due to tuberculosis was twice as frequent in men as in women. There was 1 death (male) in persons up to the age of 44 years during the 4-year period; half the deaths occurred in persons older than 70 years. Tuberculosis mortality during the last 2 years was lower than in the first 2 years of the study, and amounted to approximately 6-8 per 100 000 inhabitants.

For the sake of completeness, all deaths (due to tuberculosis or other causes) in persons registered as having active or inactive pulmonary or extrapulmonary tuberculosis, or fibrotic lung lesions, are listed in Appendix Table 14.

III. THE EPIDEMIOLOGICAL IMPACT OF MASS TREATMENT

The methods and duration of treatment for patients with active *pulmonary* tuberculosis discovered in the course of the study depended on the results of the bacteriological and photofluorographic investigations.

Patients found to be excreting tubercle bacilli by microscopic examination of direct smears, to be suffering from cavitary tuberculosis, or both, received treatment by a triple-drug regime (streptomycin 1 g for 6 weeks, thereafter 0.5 g; isoniazid 5 mg/kg body-weight; PAS (*p*-aminosalicylic acid) 10 g-12 g daily according to patient's weight). Drugs were administered daily. After cavity closure and sputum conversion had been achieved, treatment with isoniazid and PAS was continued in the dosage mentioned; the total period of chemotherapy amounted to 18-24 months.

Patients found to be excreting tubercle bacilli by culture only and persons with active non-bacillary tuberculosis received a two-drug regimen: for the first 3 months they received streptomycin and isoniazid and for about a further 15 months isoniazid and PAS in the doses mentioned above.

If sputum conversion or cavity closure had not been achieved within 6 months in the first group, and reversal of infectiousness within 3 months in the second group, further therapeutic management was on individual lines. The therapy was also modified for patients with primary resistance of the tubercle bacilli to one or more of the antituberculosis drugs used, and for patients with side-effects caused by the drugs.

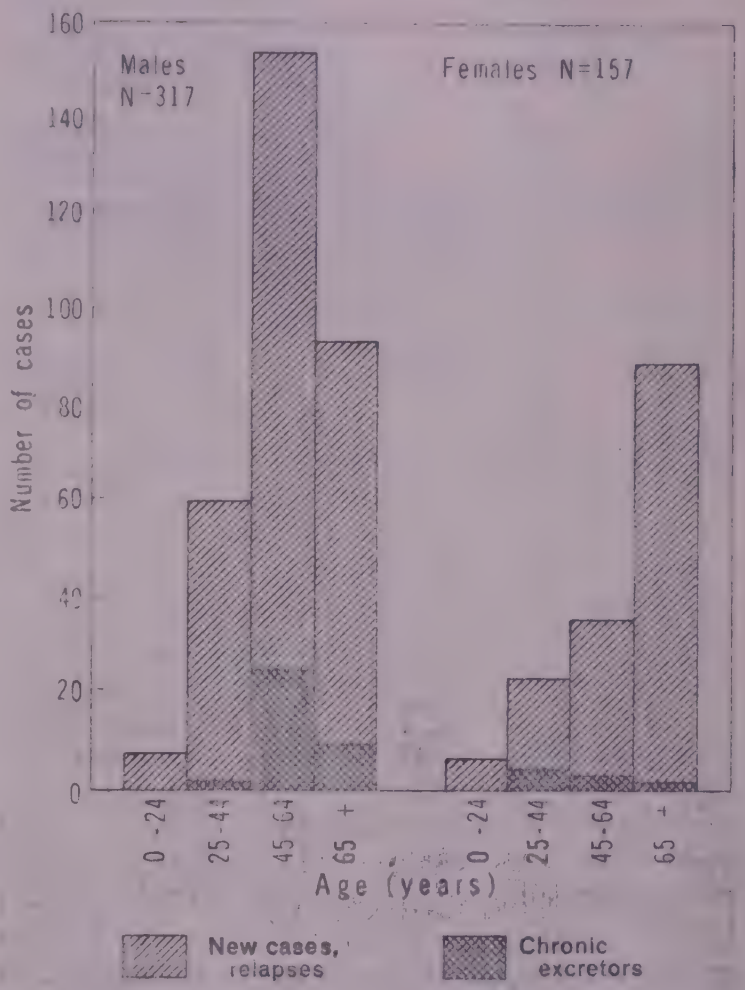
Patients who had suffered a relapse and chronic bacillary excretors were treated according to the results of sensitivity tests, as a rule by a triple regime of drugs to which bacterial sensitivity was maintained.

The therapeutic principles applied to persons with *extrapulmonary* tuberculosis did not differ substantially from those given above.

The therapeutic results obtained in 1961-64 have been evaluated for a series of 610 patients originally with active pulmonary tuberculosis. For 474 of these (78%), the diagnosis was verified by demonstration of tubercle bacilli. The 474 cases of bacillary tuberculosis comprised 348 new cases, 80 cases of relapse, and 46 chronic cases. The distribution according to age and sex is shown in Fig. 12. Only 21% of the patients were aged up to 45 years; most

FIG. 12

CASES OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY SEX, AGE AND TYPE OF DISEASE [a]



[a] The number of persons investigated, N, is given above each histogram; 23 patients in whom the duration of hospitalization was not evaluated are excluded; for details see p. 841.

males were aged between 45 years and 64 years, and most women over 65 years.

The bacteriological and photofluorographic data on the 474 patients with bacillary tuberculosis at the start of the treatment are given in Appendix Table 15. Tubercle bacilli were demonstrated in 159 patients (34%) both by direct microscopy and by culture, in the remainder by culture only. Mycobacterial resistance to one or more of the three standard drugs was demonstrated in 16% of the strains investigated. Minimal lesions were found in 25% of the cases, moderately advanced in 56%, and far advanced in 19%—lesions were classified according to the scheme current in the USA (Na-

tional Tuberculosis Association, 1961); cavitation was present in 39% of the cases.

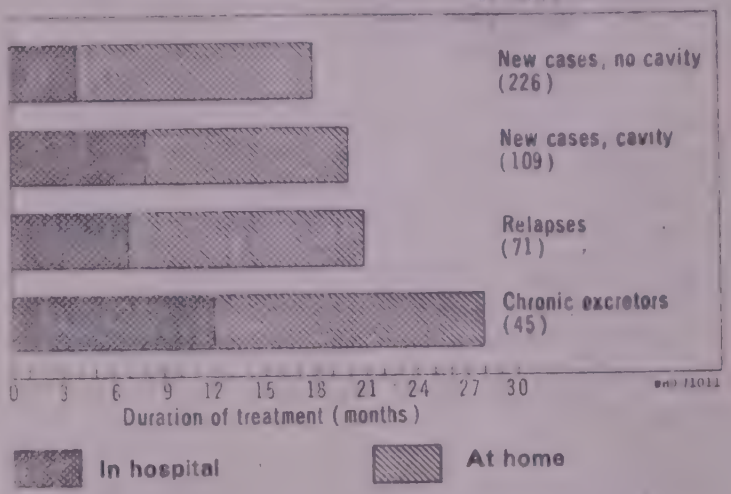
Routine treatment

An essential condition for success in the treatment of tuberculosis is that the antituberculosis drugs prescribed are really taken. The treatment regimen adopted in 1960 was therefore based on systematic hospitalization of all patients with active tuberculosis, since past experience had shown that ambulatory chemotherapy involving self-administration does not generally achieve optimal results. The unreliability of self-administration was confirmed during the present study: it was found that in spite of considerable individual education during the hospital and ambulatory treatment, about 43% of the patients who were at home did not take their PAS regularly, and about 18% did not take their isoniazid regularly. In hospitalized persons the regularity of administration of drugs was substantially better; but even with in-patients, urine analysis did not confirm the presence of the prescribed PAS in 14% of the cases, and of the isoniazid in 4%. Hospitalization at the start of the treatment was also given priority in order to remove the source of infection immediately after discovery of the disease. In addition, we wanted every patient to receive streptomycin as well as isoniazid at the start of the treatment, because the administration of streptomycin is easily supervised, and streptomycin is tolerated better than PAS; daily ambulatory administration of streptomycin in rural districts on a mass scale would have been difficult to carry out. A less serious reason for hospitalization was the relatively high mean age of the patients who, on account of bad memory and associated complaints, could not be relied upon to take the correct daily dosage at home.

The mean duration of the hospital and ambulatory treatment is presented in Fig. 13 (for full details see Appendix Table 16). For patients with newly discovered non-cavitary bacillary tuberculosis found to be excreting tubercle bacilli by culture only, who formed two-thirds of all new bacillary cases, the hospital stay lasted about 4 months, during which period they received isoniazid and streptomycin. After discharge from hospital, ambulatory treatment was continued with isoniazid and PAS for an average period of 14 months. In the remaining third of the patients with newly discovered bacillary tuberculosis, the average length of the stay in hospital was 8 months, during which period they received isoniazid, streptomycin and PAS; ambulatory treatment with a combination of isoniazid and PAS was continued for a further 12 months. In 71 patients with bacillary relapse, the average duration of hospital treatment was 7 months. During this period they underwent a triple-drug regimen, which took sensitivity-test results into account. Chronic bacillary excretors will be discussed in the next subsection.

FIG. 13

AVERAGE DURATION OF HOSPITAL AND AMBULATORY TREATMENT OF 451 PATIENTS WITH BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY TYPE OF DISEASE


New cases, no cavity (226)
New cases, cavity (109)
Relapses (71)
Chronic excretors (45)
0 3 6 9 12 15 18 21 24 27 30
Duration of treatment (months)
In hospital
At home

The duration of hospitalization was not evaluated for 23 patients (5%) of the 474 with bacillary tuberculosis; 9 (2%) of these refused hospital treatment, and the remaining 14 patients died from causes other than tuberculosis shortly after admission to hospital.

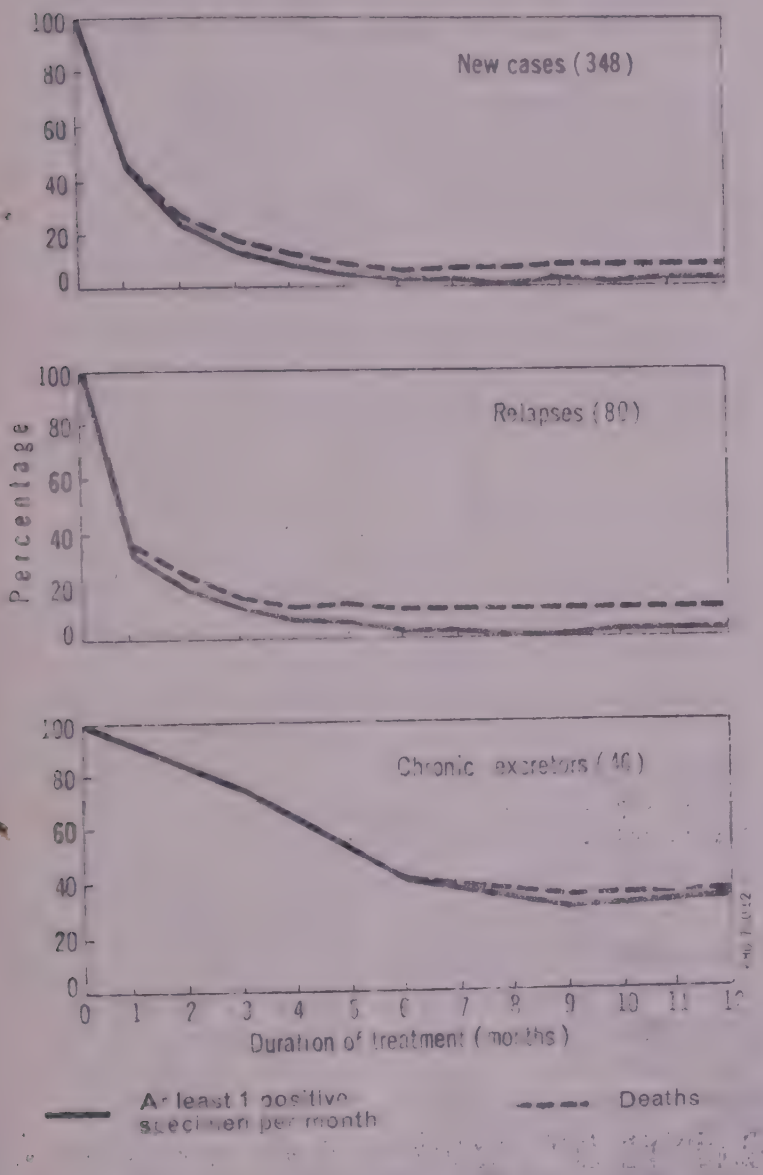
Appendix Table 16 also gives data on persons with active non-bacillary tuberculosis discovered during the same period, for the sake of comparison.

The course of sputum conversion during the first 12 months of chemotherapy for patients with bacillary tuberculosis in the years 1961-64 is shown in Fig. 14.

Of the 348 patients with newly discovered bacillary tuberculosis, 41 (12%) were found to be excreting tubercle bacilli after 3 months' treatment, and only 3 (1%) after 6 months' treatment. Only 2 persons failed to achieve bacteriological quiescence: one man was found to be excreting *Myco. tuberculosis* var. *avium* resistant to both standard and secondary antituberculosis drugs (with the exception of cycloserine); and one woman was found to be excreting *Myco. tuberculosis* var. *hominis* sensitive to all three standard drugs, but long-term adequate treatment could not be carried out because of serious drug

FIG. 14

PERCENTAGE OF PATIENTS WITH AT LEAST ONE POSITIVE CULTURE PER MONTH, AND PERCENTAGE OF PATIENTS DYING, IN KOLN DISTRICT IN 1961-64, BY TYPE OF DISEASE AND DURATION OF TREATMENT



intolerance. Mycobacteria also appeared transitorily in the sputum of 4 patients between the sixth and twelfth months after the start of treatment, and in a further 3 persons in the second or third year. A total of 27 patients (18%) died during the first year of treatment; with one exception, sputum conversion had been achieved in all patients a short time before death.

Of the 80 patients who had suffered a relapse, 9 (11%) were found to be excreting tubercle bacilli after 3 months' treatment. The form of the curve showing the course of sputum conversion is similar to that for the newly discovered cases. Transitory positivity was demonstrated in 2 patients. Treatment was unsuccessful in only 1 patient, in whom mycobacterial resistance developed against both standard and secondary antituberculosis drugs, and who hence became a chronic bacillary excretor. In the first year of treatment, 8 persons (10%) died; mycobacteria were no longer found at the time of death.

The curve for the chronic excretors, also shown in Fig. 14, will be discussed in the next subsection.

The series of patients with active non-bacillary tuberculosis comprised 125 persons with newly discovered disease and 11 persons who had suffered a relapse. Treatment results were evaluated here according to changes in the radiographic and clinical pattern only. In view of the fact that this group is of little importance from the public health angle, detailed results are not presented. One indication of the success of the treatment is that in no instance were tubercle bacilli found in the sputum after the termination of the chemotherapy.

Treatment of chronic bacillary excretors

Patients with chronic bacillary tuberculosis present one of the most serious contemporary problems of tuberculosis control the whole world over, not only from the epidemiological but also from the therapeutic, social and economic viewpoints. Our main object here was to prevent as far as possible the emergence of new chronic bacillary excretors by systematic, adequate treatment of all patients with newly discovered tuberculosis and all those who had suffered a relapse. Adequate treatment was also given to all existing chronic bacillary excretors.

At the start of the study there were 53 patients—44 men (83%) and 9 women (17%)—answering to our definition of chronic bacillary excretors (uninterrupted excretions of tubercle bacilli for a period of 2 years or longer). In 1961, 10 more chronic excretors (5 men and 5 women) were discovered, in 1962 2 men, and in 1963 again 2 men, a total of 14 patients altogether. No new chronic bacillary cases were discovered in 1964. The average age of the patients was 55 years.

As compared with the other patients registered as having bacillary tuberculosis at the start of the study, chronic bacillary excretors generally had lesions of a more serious nature; mycobacteria resistant to isoniazid, streptomycin and PAS were more frequently demonstrated (this is discussed in more detail in the next subsection); tubercle bacilli were found by microscopy in a higher percentage of direct sputum smears; and cavitation was more frequently present (Appendix Table 15). However,

careful examination of the clinical records showed that the unfavourable situation of chronic bacillary excretors did not arise because the original lesions differed from the lesions of the remaining patients registered in the group of bacillary tuberculosis, but in most cases as a result of inadequate antimicrobial treatment, for which the patient or the physician was responsible.

The treatment regimen we adopted was based on the sensitivity of the mycobacteria to the antituberculosis drugs. If mycobacterial resistance to one or more standard antituberculosis drugs was demonstrated, the drug or drugs concerned were replaced by secondary antituberculosis drugs (ethionamide, pyrazinamide, viomycin, cycloserine). If the results of mycobacterial-sensitivity tests for isoniazid, streptomycin and PAS were not available, the combination used was based on the history of previous drug treatment.

Treatment of chronic bacillary excretors was always started in hospital, where they stayed for 1 year on the average; ambulatory chemotherapy was continued for a further 16 months on the average (Fig. 13 and Appendix Table 16). The value of admission to hospital for these patients is revealed by the fact that tests for the presence of antituberculosis drugs in the urine demonstrated irregularity in taking the secondary antituberculosis drugs in approximately one-quarter of the patients receiving ambulatory chemotherapy by pyrazinamide, ethionamide or cycloserine.

Fig. 14 shows that bacteriological quiescence was achieved more slowly in chronic bacillary excretors than in persons with newly discovered tuberculosis or in relapse.

The over-all balance as regards chronic bacillary tuberculosis for the period from the start of the study (1 October 1960) to 31 December 1964 is shown in Table 12.

In the course of rather more than 4 years, the number of chronic bacillary excretors declined from 53 to 8, i.e., by 85%. This decrease was due to two factors:

(*a*) the total mortality in chronic bacillary excretors from tuberculosis and other causes (22) was in excess of the incidence of new chronic cases (14), and

(*b*) treatment with secondary antituberculosis drugs cured many patients.

Bacteriological quiescence was achieved in 42 patients (37 living on 31 December 1964 and 5 died, sputum negative) out of a total of 60 patients, i.e., in 70% of those treated. We excluded from the evaluation of the results of treatment 4 persons who did not receive adequate treatment at the start of the study, on account of serious associated disease leading to death, and a further 3 persons who died during the first 3 months of the study.

TABLE 12

HISTORY OF CHRONIC BACILLARY EXCRETORS IN KOLÍN DISTRICT BETWEEN THE START OF THE STUDY (1 OCTOBER 1960) AND 31 DECEMBER 1964

	1.10.1960	1.10.60-31.12.64	Total
No. of chronic bacillary excretors registered	53	14	67
Died before 31 December 1964 from			
tuberculosis, sputum positive	12	1	13
tuberculosis, sputum negative	1	—	1
other causes, sputum positive	3	1	4
other causes, sputum negative	4	—	4
Total deaths	20	2	22
Living on 31 December 1964	33	12	45
Reversal of infectiousness			
obtained in	27	10	37
not obtained in	6	2	8

A further reduction in the number of chronic bacillary excretors in Kolín district may be expected only if we succeed in limiting the emergence of new chronic bacillary excretors to the minimum by systematic, adequate treatment of all newly discovered cases and cases of relapse.

Mycobacterial resistance to antituberculosis drugs

Tests of mycobacterial sensitivity to isoniazid, streptomycin and PAS were carried out routinely for all isolated strains. The results of sensitivity tests are lacking only where subcultures of the strain failed to grow, or where tests were made in other laboratories by other techniques.

In 1961-64, sensitivity tests were evaluated for 473 (92%) of the 512 patients with bacillary tuberculosis (Appendix Table 17).

Primary resistance was found in 13 (4%) of the 327 persons with newly discovered bacillary tuberculosis. A closer analysis revealed that in 4 persons secondary resistance to some antituberculosis drugs previously administered for other reasons than active tuberculosis could not be excluded. We may safely

classify mycobacterial resistance against antituberculosis drugs as primary only in 9 persons (3%); in the majority of these, resistance was found against only one drug; one of the 9 patients excreted *Myco. avium* resistant to all antituberculosis drugs both standard and secondary (with the exception of cycloserine).

The frequency of *secondary* resistance in relapsed patients differed from that in chronic bacillary excretors. In relapsed patients it was found in only about one-third of the cases, mostly as resistance to isoniazid alone. The low number of relapsed patients with mycobacterial resistance to streptomycin may be explained by the fact that streptomycin was never used in Czechoslovakia for persons receiving ambulatory treatment. In contrast, mycobacterial resistance to standard antituberculosis drugs was found in 83% of chronic bacillary excretors. Most strains were resistant to two or all three antituberculosis drugs.

The incidence of resistant strains found in persons with bacillary tuberculosis decreased between 1961 and 1964 (Appendix Table 18). In 1961, mycobacteria resistant to one or more of the three standard antituberculosis drugs were isolated from 18 persons (11%); in 1964 only 4 resistant strains (6%) were found. This reduction was caused on the one hand by the fact that the absolute number of newly discovered cases and relapses declined, and hence the probability of the emergence of resistant strains in the two groups likewise declined, and on the other hand by the fact that adequate chemotherapy reduced to a minimum the number of chronic bacillary excretors. Not a single case of mycobacterial resistance to isoniazid, streptomycin or PAS developed in the course of the study in the 327 persons with newly discovered bacillary tuberculosis whose sensitivity tests could be evaluated. One case developed among the 73 persons with tuberculosis relapse.

TABLE 13

ANNUAL PREVALENCE OF PERSONS WITH MYCOBACTERIA RESISTANT TO AT LEAST ONE ANTITUBERCULOSIS DRUG IN KOLÍN DISTRICT IN 1961-64

Year	Prevalence	
	No.	% [a]
1961	60	27
1962	36	25
1963	21	16
1964	14	16

[a] Percentage of total prevalence of bacillary tuberculosis.

The decrease in the prevalence of persons excreting resistant mycobacteria during the 4 years of the study is shown in Table 13.

The majority of the patients discharging tubercle bacilli resistant to the drugs in 1964 were chronic excretors. The results reveal that with adequate, timely treatment drug-resistance ceases to be a serious problem.

IV. THE RISK OF DEVELOPING TUBERCULOSIS

POPULATION GROUPS CONSIDERED

The results of the study for the first 4 years of its operation make it possible to determine (for this period) the risk of developing pulmonary tuberculosis in the following population groups:

(*a*) persons registered as having fibrotic lesions in the lungs,

(*b*) persons registered as having inactive tuberculosis,

(*c*) persons over 14 years of age with previously normal chest X-ray findings,

(*d*) children up to 14 years of age.

The incidence of bacillary tuberculosis in the various groups during the 4 years in question showed wide variations, as may be seen from Table 14.

TABLE 14

AVERAGE ANNUAL FREQUENCY OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64

Group	No. of persons	Annual frequency	
		No.	% [a]
Inactive tuberculosis	1 500	20	1.3
Fibrotic lung lesions	3 500	27	0.8
Negative chest X-ray, over 14 years	73 000	60	0.08
Total	78 000	107	0.14
Children, up to 14 years	22 000	0.5	0.002

FIBROTIC LESIONS AND INACTIVE TUBERCULOSIS

Cases of bacillary tuberculosis were diagnosed with the greatest relative frequency in persons registered as having inactive tuberculosis or fibrotic lesions in the lungs. In the period 1961-64, an average of 47 cases per year of bacillary tuberculosis (i.e., nearly 44% of all newly detected bacillary cases) were found in this group of 5000 persons. By contrast, an average of 60 cases of bacillary tuberculosis (nearly 56%) originated among the 73 000 persons over 14 years of age with previously normal chest X-ray findings. The incidence of bacillary tuberculosis among children up to 14 years of age was very low indeed, and did not rise above 1 case per 2 years (about 0.5%).

The risk of developing bacillary tuberculosis in persons registered as having inactive tuberculosis is dealt with in the section on relapses (pages 837-839).

The number of persons with fibrotic lesions in the lungs and their distribution according to sex and age at the start of the study (1960), after the first mass investigation of the inhabitants (1961), and after the study had been in operation for 4 years (1964) are presented in Appendix Table 19. It will be seen from this table that a large number of previously unknown cases of fibrotic lesions were found in the course of the first mass photofluorographic survey of the inhabitants in 1961, when the number of persons registered as having these lesions rose to twice that at the start of the study. The percentage prevalence in both sexes rose continuously with age, attaining approximately 15% in males over 75 years of age in 1964, and 9% in the corresponding female group.

The risk of developing bacillary tuberculosis for persons with fibrotic lesions is shown in Table 15.

In the period 1951-64 bacillary tuberculosis was detected in 107 persons registered as having fibrotic lesions in the lungs; the mean annual risk of developing the disease amounted to approximately 1% in males and 0.6% in females; the difference is statistically significant.

A more accurate estimate of the risk in this group will be possible after a lengthier period of observation, when the influence of some accidental factors will have been practically totally excluded, as for example mistaking " fibrotic " lesions for active abacillary tuberculosis; at the same time the correlation between the risk of disease in these persons and age and some further factors will be more clearly defined.

NORMAL PERSONS OVER 14

In the large group of 73 000 persons older than 14 years with previously normal chest X-rays, 241 cases of bacillary tuberculosis were found during the first 4 years of the study, i.e., an average of 60 cases annually (Table 14). The average annual risk of developing bacillary tuberculosis in the years 1961-64 was 0.1% in males and 0.06% in females, and was approximately 10 times lower than for persons with fibrotic lesions in the lungs.

The correlation between the incidence of the disease and the following factors was determined:

(*a*) sex and age,
(*b*) contact with human sources of infection,
(*c*) contact with bovine sources of infection, and
(*d*) previous BCG vaccination.

Sex and age

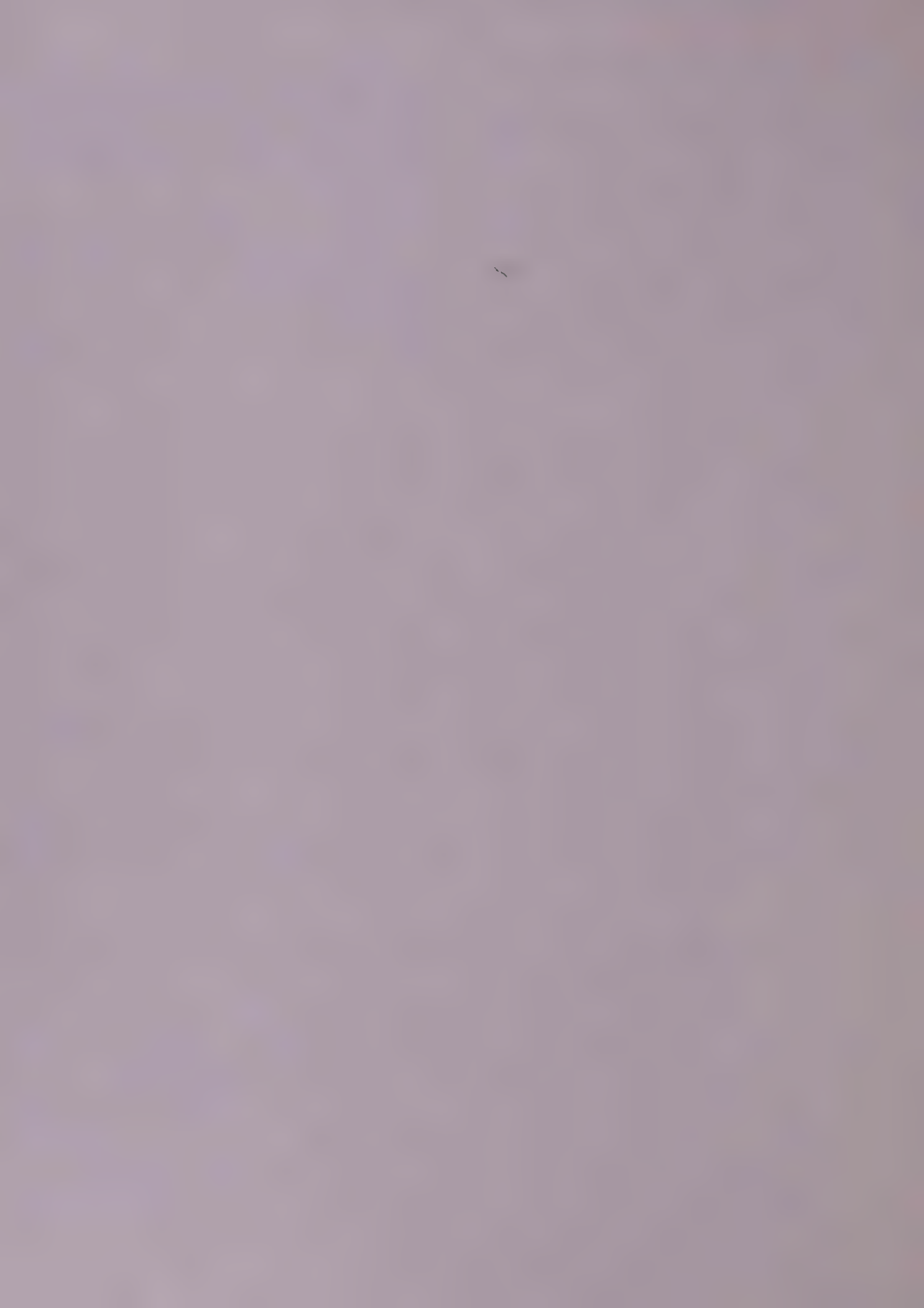
An analysis of the distribution of cases of bacillary tuberculosis according to sex and age has been given in the section on incidence.

TABLE 15

INCIDENCE OF BACILLARY TUBERCULOSIS IN 1961-64 AMONG PERSONS WITH FIBROTIC LUNG LESIONS IN KOLÍN DISTRICT

Sex	Incidence									
	1961		1962		1963		1964		1961-64	
	No.	%[a]	No.	%[a]	No.	%[a]	No.	%[a]	No.	%[a]
Male	13	1.3	15	0.8	25	1.3	16	0.8	69	1.0
Female	6	0.7	14	0.8	9	0.5	9	0.5	38	0.6
Total	19	1.0	29	0.8	34	0.9	25	0.7	107	0.8

[a] Percentage of persons registered for fibrotic lung lesions.



Contact with human sources of infection

The introduction of systematic antimicrobial therapy in hospital for all known cases of active tuberculosis in the Kolín district substantially reduced the period in which there was an infection risk for contacts after discovery of bacillary tuberculosis. At the end of 1964, there remained in the whole district only 8 known persistent sources of infection—patients with chronic tuberculosis did not respond to treatment. The risk of infection, of contacts, therefore, was only significant up to the time when the disease was discovered.

The incidence of bacillary tuberculosis in family contacts of patients with bacillary tuberculosis is presented in Table 16.

TABLE 16

NEW CASES OF BACILLARY TUBERCULOSIS AMONG FAMILY CONTACTS OF PATIENTS WITH BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64

Year	New cases of bacillary tuberculosis among family contacts		Year when source of infection was positive				
	No.	%	1960	1961	1962	1963	1964
1961	2	0.41	2	—	—	—	—
1962	4	1.48	1	—[a]	3	—	—
1963	—	—	—	—	—	—	—
1964	2	1.28	—	—	1	1	—
Total	8	0.55	3	—[a]	4	1	—
No. of family contacts			253	439	272	253	157

[a] Active non-bacillary tuberculosis was diagnosed in two family contacts in 1962; both the sources of infection involved were positive in 1961 only.

This table reveals that bacillary tuberculosis was found on an average in 0.55% of family contacts; in most cases the disease was contracted within two years after the discovery of the source of infection, despite the fact that this source was promptly isolated and rendered non-infectious. We believe that infection probably took place prior to the discovery of the source of infection, although tuberculosis in the family contacts generally became manifest more than 12 months after the removal of the source.

Contact with bovine sources of infection

The significance of bovine tuberculosis for the spread of infection in a vaccinated population has not yet been reliably established, mainly because no suitable method is available for distinguishing a population infected with *Myco. tuberculosis* var. *bovis* from one with *Myco. tuberculosis* var. *hominis*. Reliable differentiation between the two kinds of infection is feasible only for the relatively limited group of persons with bacillary tuberculosis.

From the start of the study (1 October 1960) up to the end of 1964, mycobacteria could be isolated from a total of 608 cases; in 25 (21 males and 4 females) of these (4.1%), *Myco. tuberculosis* var. *bovis* was demonstrated). Of these 25 persons, 22 had pulmonary and 3 extrapulmonary disease. Occupational contact with sources of infection could be reliably established for 13 persons; this means a mean annual risk of contracting bacillary tuberculosis of 0.22% for the 1500 persons exposed to bovine tuberculosis.

BCG vacccination

In Czechoslovakia, where mass BCG vaccination has been carried out since 1949, no reliable studies on the correlations between the incidence of tuberculosis and BCG vaccination are possible. At the most, we can establish the present incidence of tuberculosis in vaccinated and unvaccinated subjects at ages from 0 to 34 years; BCG vaccination in these subjects using either Danish or Czechoslovak vaccine dates back 15 years.

During the first 4 years of the Kolín study, bacillary tuberculosis was found in only one child, aged 14 years; this child was BCG-vaccinated. In the age-group 15-34 years, a total of 31 persons was found to be suffering from bacillary pulmonary tuberculosis. Of these, 12 had received vaccination against tuberculosis in previous years, and 15 had not been vaccinated; no information on BCG vaccination was available for 4 persons. The annual incidence of tuberculosis amounted to 0.026% in the 11 636 vaccinated and to 0.092% in the 4073 unvaccinated persons with positive Mantoux tests. For the 7029 persons for whom no information on BCG vaccination was available, the incidence was 0.014%.

CHILDREN UNDER 14

As revealed by Table 14, the annual incidence of bacillary tuberculosis in children aged up to 14 years was very low indeed. We attempted to ascertain

the risk of developing active tuberculosis in vaccinated children whose tuberculin allergy increased by at least 12 mm between two tuberculin tests from a reading of 0-5 mm in 1961. These children were submitted to annual bacteriological and radiographic investigations. Such an increase in tuberculin allergy was found during the first two years of the study in 88 among 13 000 schoolchildren; in none of these was any evidence of active tuberculosis discovered up to the end of 1964.

CONCLUSION

We have been able to show that the risk of developng tuberculosis in the group of 73 000 persons with nitially normal chest X-rays varied according to sex and age; men over the age of 45 years and women over the age of 65 years should be considered—from these results—to run the highest risk. We were also able to throw light on the effect of some other factors on the origin of tuberculosis, particularly of contact with human or animal sources of infection. The tuberculosis incidence was higher than the average in persons thus exposed; but only small groups were affected, and their numerical strength and epidemiological significance will continue to decline with the elimination of human and animal sources of infection. The effect of BCG vaccination on the risk of developing tuberculosis was substantially as found in other trials: the risk was approximately four times higher among non-vaccinated subjects than in BCG-vaccinated ones.

V. ECONOMIC ASPECTS

The total cost of operating a tuberculosis control programme is of paramount importance. As it is very difficult to list all direct and indirect items of expenditure involved in the control of tuberculosis in Kolín district during the 1961-64 period, we shall limit our data to some objective indicators, which may be relatively simply compared with those from other districts of Czechoslovakia or from other countries. These include the mean duration of institutional treatment for cases of active tuberculosis, the mean daily requirement of beds for the treatment of tuberculosis, the number of ambulatory patients receiving antituberculosis drugs, and the drug consumption for institutional and ambulatory treatment. We have also included the duration of incapacity for work and the number of disability pensions granted on account of tuberculosis; however, these indicators are generally comparable only within a given country, as they depend to a marked degree on the social security provided for tuberculous patients, the economic system in force, etc.

Detailed data on the duration of hospital treatment for persons with active tuberculosis for the 4 years of the study are given in the previous section and in Appendix Table 20. The mean duration was 5 months for new cases, 7 months for relapses and 1 year for chronic cases of tuberculosis. During the period under review no substantial change occurred in the duration of hospital treatment for these categories of patients; this means that the reduction in the number of beds required which was achieved in Kolín district during the 4-year study period—referred to below—was not influenced by changes in the duration of hospital treatment.

Comparison of the data for 1961 and 1964 reveal a reduction of the daily requirement of beds for treatment of newly discovered and relapsed cases of tuberculosis by 44%, the number required for treating chronic tuberculosis cases decreasing by as much as 88%. The daily requirement of beds was determined by assuming a 90% mean rate of occupation, and the duration of institutional treatment referred to above (Appendix Table 20 and Fig. 15). The greatest number of beds (130) was required in 1961, mainly as a result of the first photofluorographic survey of the population and the hospitalization of all chronic excretors. In 1963, despite the repetition of the mass investigation of the population, the mean daily requirement of beds declined to 83; this was further reduced to 58 beds in 1964.

A simultaneous reduction was found in the number of persons receiving ambulatory treatment; on 31 December 1961 a total of 393 persons were undergoing ambulatory chemotherapy, in 1964, however, only 141—i.e., about 36% of the original figure.

The quantities of standard and secondary antituberculosis drugs dispensed to patients in hospital and by the clinics are set out in Appendix Tables 21 and 22 and in Fig. 16. After a rise from 1961 to 1962, the amount of the various drugs used fell, and was generally less in 1964 than in 1961. The amounts

FIG. 15
AVERAGE DAILY REQUIREMENT OF HOSPITAL BEDS FOR ACTIVE TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64, BY TYPE OF DISEASE

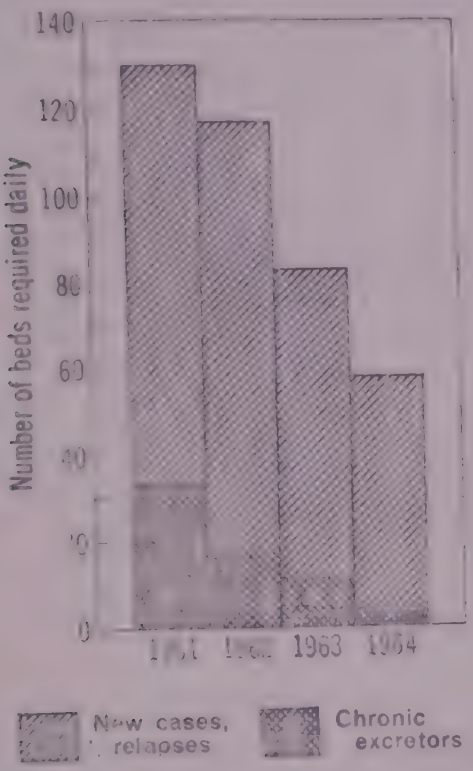
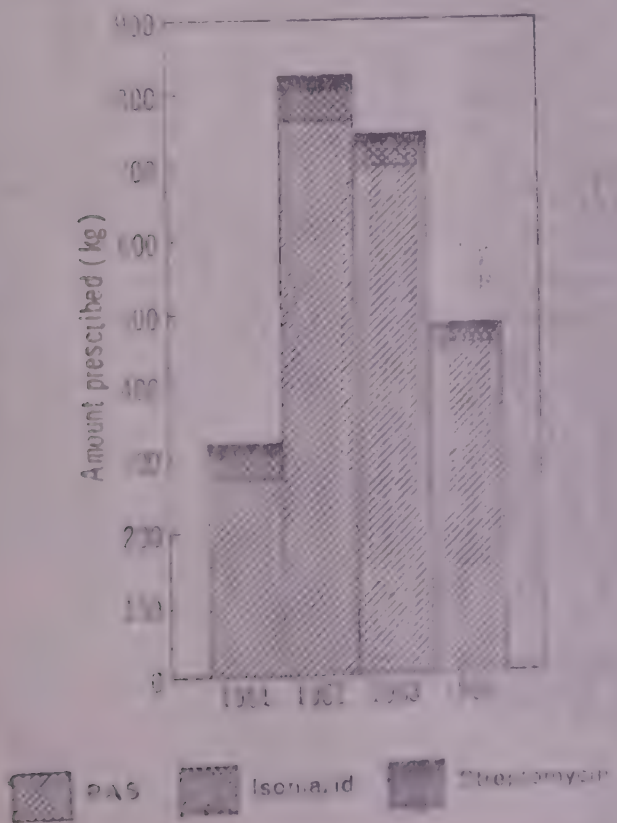


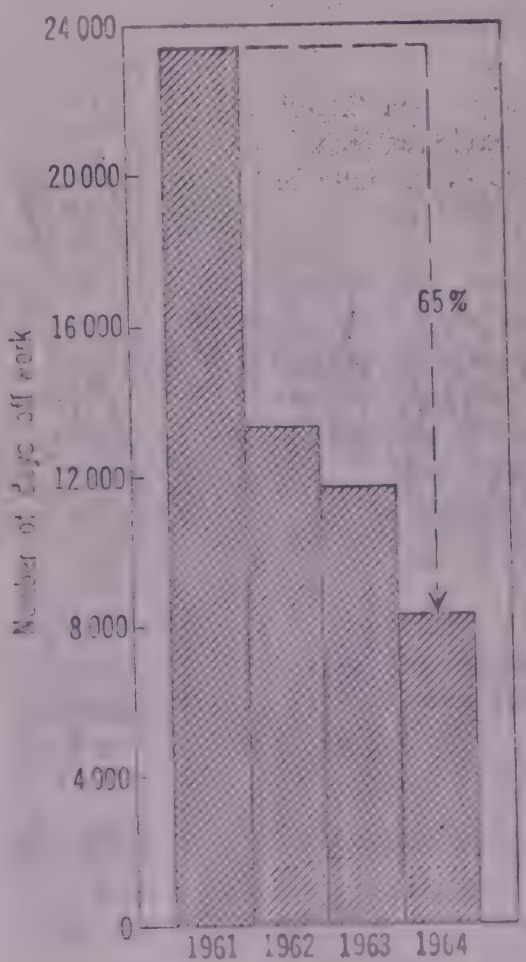
FIG. 16
AMOUNTS OF STREPTOMYCIN, ISONIAZID AND *P*-AMINOSALICYLIC ACID (PAS) PRESCRIBED ANNUALLY FOR PATIENTS WITH ACTIVE TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64



of streptomycin and isoniazid used in 1964 were about half those required in 1961; a reduction by about one-quarter was found in the requirement for ethionamide. The amount of PAS used in 1964 was, however, more than in 1961; its consumption during the first year of the study was relatively low, as in two-thirds of the newly discovered cases of tuberculosis treatment was initiated with a two-drug regimen of isoniazid and streptomycin. The same applies to pyrazinamide, which was used as a substitute for PAS in case of side-effects produced by the latter.

The mean duration of incapacity for work due to tuberculosis among newly discovered cases and relapses fluctuated between 199 and 246 days, i.e., 6 and 8 months, in 1961-64, confirming that the length of treatment decided on in the study protocol was generally strictly adhered to. Patients with newly discovered tuberculosis returned to work after an average absence of 7 months, and patients

FIG. 17
LOSS OF WORKING TIME DUE TO NEW CASES AND RELAPSES OF TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64



who had suffered relapse after 8 months, as a rule resuming their original occupation (Appendix Table 23).

A good indicator of the economic benefits of tuberculosis control in Kolín district is provided by data on the number of working days missed owing to pulmonary tuberculosis in the successive years of the study, as shown in Fig. 17. In 1961 a total of 24 282 working days were missed in Kolín district on account of newly discovered tuberculosis and relapses. This figure had already dropped by 40% in 1962 and was further reduced by 12% of the original number in each of the two following years. This means that the total number of working days missed on account of tuberculosis had dropped by 65% in 1964 as compared with 1961.

Disability pensions for tuberculosis were granted, during the four years of the study, to 19 (12.2%) of the 155 persons with newly discovered pulmonary tuberculosis who were in regular employment at the time of diagnosis, and to 14 (20.0%) of the 70 persons who suffered a relapse. Apart from this, additional disability pensions for tuberculosis were granted to another 24 persons whose tuberculosis had been discovered before the commencement of the study, or who were suffering from extrapulmonary tuberculosis. This means that a sum total of 57 persons were granted disability pensions for tuberculosis during the four-year period under review, i.e., an average of 14 persons annually (Appendix Table 24), corresponding to a rate of 34.8 per 100 000 persons eligible for the pensions scheme. Like the other epidemiological indices, the number of disability pensions granted on account of tuberculosis rose from 1961 to 1962 and then fell steadily, being only about half as much in 1964 as in 1961.

VI. DISCUSSION AND CONCLUSIONS

PREVALENCE TRENDS

As may be seen from Table 5, the total prevalence of bacillary tuberculosis nearly doubled from 1960 to 1961, as a result of the first mass survey of the population in 1961, and then showed a continuous, fairly rapid decline, in spite of the fact that the mass survey was repeated in 1963. This trend was accompanied by a striking change in the composition of the group of bacillary tuberculosis patients: the number of newly discovered cases of tuberculosis (the incidence) increased during each mass survey of the population and was just as large at the end of the study as at the beginning, while in particular the number of chronic excretors showed a steady decline. The above-mentioned increase in the incidence was due to the increased detection of cases found by culture only to be excreting tubercle bacilli (these numbered 99 in 1961 as compared with 16 in 1960; similarly 48 in 1963 compared with 20 in 1962). In contrast, the number of new cases with tubercle bacilli demonstrated by microscopy of sputum remained practically unchanged during the first mass photofluorographic investigation, and even declined during the second survey, probably as a result of the detection of so many previously unknown sources of infection in the course of the first mass X-ray investigation and their adequate treatment.

The adequate chemotherapy of all persons with active tuberculosis during the first four years of the study led to a most striking reduction in the prevalence of chronic bacillary excretors with microscopic evidence of tubercle bacilli in the sputum, of whom only 5 remained in 1964 as against 42 in 1960. This reduction was due to the fact that the majority of chronic bacillary excretors known at the start of the study (of the 42 only 4 were still microscopically positive in 1964) were rendered non-infectious by secondary antituberculosis drugs while only 14 new cases of chronic bacillary tuberculosis arose during the period under review. In fact, only 2 cases of chronic bacillary tuberculosis came from the total of 428 newly discovered bacillary cases and relapses during the first four years of the study, whereas the remaining 12 chronic bacillary excretors were recruited from patients who received inadequate chemotherapy before the start of the study and were not designed as chronic bacillary excretors according to the accepted definition until 1961 (10 cases) or 1962 (2 patients).

The proportion of chronic bacillary excretors in the total prevalence of microscopically positive cases constitutes an important indicator of the dynamics of bacillary tuberculosis and of the standard of the control measures applied. It amounted to 53% at the start of the study and to only 15% after 4 years. The cause of this surprising reduction was the fact that during the study, with adequate chemotherapy, only about 0.5 new chronic excretors emerged annually from all new cases of active

tuberculosis (2 persons in 4 years); on the other hand, 10 cases annually at least had to be assigned to this group during the several years preceding the study. The group of chronic bacillary excretors found by microscopy was reduced by 37 in 4 years, reversal of infectiousness being achieved mainly during the first 2 years, while 22 persons in this group died. In contrast, up to 1960 any reduction in the number of chronic excretors was practically only a result of mortality. Accordingly, persons with this epidemiologically most significant form of tuberculosis continued to accumulate, making up more than half of the total prevalence of microscopically positive cases of bacillary tuberculosis at the start of the study.

The number of all cases except chronic bacillary excretors with tubercle bacilli found by microscopic sputum examination fell only from 38 to 29 during the study, i.e., by only about 25%. This reflects the fact that a certain proportion of new cases reached the microscopically positive bacillary stage so rapidly that they could not be prevented through the described system of treatment. Chemotherapy had an indirect effect on the incidence of bacillary tuberculosis, as adequate treatment led on the one hand to a reduction of exogenous infection, and on the other to a decrease in the risk of relapse.

The striking decrease in the number of chronic bacillary excretors in the period 1961-64 might be thought to make this group the most interesting one for the future planning of tuberculosis control programmes, as this study has shown that adequate chemotherapy of newly notified cases, relapses and chronic cases greatly reduces the number of chronic cases.

However, the group of new cases detected by direct smear microscopy is even more important. Persons in this group are the main sources of human infection, and many of them become chronic bacillary excretors if not given adequate chemotherapy. There is still a strong feeling among physicians that the number of persons with undetected tuberculosis discharging tubercle bacilli demonstrable by direct smear microscopy can be drastically reduced by mass photofluorography. The results of this study indicate that this may not be the case.

PROGNOSIS

We reached the conclusion, on the basis of the analysis presented, that we may expect only a less marked decline in the prevalence of bacillary tuberculosis with tubercle bacilli in the sputum demonstrated by microscopy during the ensuing years in the district under study. This is borne out by the following considerations.

1. In the course of the next few years only a small reduction of the number of chronic bacillary excretors can be counted on, in view of the fact that only 5 "good" chronic excretors were alive in 1964 in the district studied; reversal of infectiousness cannot be achieved for them because of multiresistant tubercle bacilli or contraindications to the application of suitable drugs, and their prolonged survival may be expected as a result of the good standard of general health care.

2. Likewise, relapses can be expected to undergo only a very gradual reduction, mainly because the inactive tuberculosis pool still contains approximately 1000 persons, most of whom received inadequate treatment in the past, and who thus represent a relatively high relapse risk. The risk of relapse is very low in persons who have completed adequate therapy, and judging from past experience does not differ much from the risk of disease in healthy persons.

3. The number of new cases of bacillary tuberculosis arising from the group of persons with fibrotic lung lesions is likewise likely to decline only slowly, approximately in proportion to their total number, which is at present about 3600 per 100 000 population (Appendix Table 19) and is decreasing by about 150 per 100 000 annually; no marked change from the present tuberculosis rate from this group (1% in males, 0.6% in females annually), is thus expected in the near future.

4. A very slight decline has been noted in the incidence of microscopically positive bacillary tuberculosis in persons with previously normal chest X-rays; this decline may be expected to continue, but no accurate estimate can be made of its extent.

EVALUATION OF THE METHODS OF TREATMENT USED

Least controversial is the effect of adequate chemotherapy which, on account of its pronounced effect, has developed into the most important method of tuberculosis control. In contrast, the role played by the other two important measures of tuberculosis control—photofluorographic surveys of the population and BCG vaccination of children and

adolescents—cannot be accurately estimated from results obtained so far, as these two methods influence each other. The relatively low case-yield from photofluorographic investigation in vaccinated persons was demonstrated during the first mass survey of the population, in the group of young persons vaccinated in previous years; a substantially smaller proportion of bacillary tuberculosis cases was discovered in them than in non-vaccinated persons. The limited effect of BCG vaccination in a population with only a small number of infectious sources may, on the other hand, also be observed from the results of the study; after the majority of unknown sources of infection had been discovered in 1961 and received adequate chemotherapy, the incidence of bacillary tuberculosis declined considerably.

These relatively short-term experiences already reveal the fact that the consequences of BCG vaccination and mass photofluorographic investigation of the population overlap to a considerable extent, and that the application of either of them markedly reduces the effect of the other. We believe that photofluorography as part of the case-finding programme is frequently used excessively, as it is not focussed on accurately determined risk groups in the population concerned. The first mass investigation of the population yielded a relatively large number of active and suspected cases of tuberculosis and may thus be considered as justified. In contrast, the second mass photofluorographic investigation 2 years later was a luxury from the practical angle, but necessary as part of the study.

Tuberculosis control programmes in operation in various countries differ as to methods applied, epidemiological efficacy, and funds required for results obtained.

In view of the complexity of the situation, and the continual change in parameters, it is not surprising that it should prove so difficult in technically advanced countries to overcome the superfluity of certain traditionally accepted control measures, and to achieve permanent improvement of the epidemiological situation by the optimum economic means.

DRUG-RESISTANCE

During the first 4 years of this study, primary resistance to antituberculosis drugs did not exceed 4% of all cases of active tuberculosis, in agreement with reports by many European authors (Fox et al., 1957; Rist & Crofton, 1960; Hornung & Polonczyk, 1962; Kreis, 1962; Lepeuple et al., 1963).[1] The contribution made by the Kolín study affects particularly the problem of secondary resistance, as this could be studied in a geographically well-defined region by standard methods over a relatively long period. At the start of the study the prevalence of persons harbouring tubercle bacilli resistant to at least one drug was accounted for mainly by secondary resistance, 60 per 100 000 inhabitants, whereas in 1964 this had declined already to 14 per 100 000.

RISK GROUPS

In order to determine the risk groups even more accurately, mass photofluorographic investigation of the population over 14 years of age will have to be repeated once more. However, it seems to be almost certain that the main risk group is represented by men above 45 years and women above 65 years of age. The results of the investigation of persons in the higher age-groups in the Kolín study differ from the findings of the Danish Tuberculosis Index (Groth-Petersen et al., 1959).

THE INFLUENCE OF BOVINE TUBERCULOSIS

The prevalence of bacillary tuberculosis was influenced relatively little by the incidence of bovine tuberculosis. The data on the proportion of bovine strains found in the present study, amounting to 4% in 1961-64 (25 out of the total of 608 strains isolated), tally with those obtained in Czechoslovakia (Grüner & Böhm, 1936) and some other countries (Goerttler & Weber, 1954) in the past. The absolute number of bovine strains isolated annually hardly varied from 1961 to 1964, which means that infection by *Myco. tuberculosis* var. *bovis* attained relatively greater epidemiological significance with the reduction in the number of human sources. Contact with tuberculin-positive cattle was proven in practically every case of excretion of *Myco. tuberculosis* var. *bovis*.

INFECTION IN CHILDREN

We were not able to study a very sensitive parameter, namely the incidence and prevalence of infection in children and young persons, as in Czechoslovakia mass BCG vaccination has been carried out since 1949.

[1] See also *The public health significance of drug resistance*, unpublished WHO document TB/Techn. Information/34.

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RÉSUMÉ

Depuis la fin de 1960, une enquête longitudinale portant à la fois sur l'épidemiologie et sur les aspects cliniques de la tuberculose pulmonaire est en cours en Tchécoslovaquie avec la collaboration de l'Organisation mondiale de la Santé. Le district de Kolín, comptant 190 000 habitants, a été choisi à cet effet et un nombreux personnel spécialisé a été affecté aux recherches. Avant le début des investigations, les indices épidémiologiques relatifs à la tuberculose relevés dans ce secteur ne différaient pas notablement des indices constatés dans d'autres régions de Tchécoslovaquie.

L'objectif principal de l'enquête était d'obtenir un tableau précis de la situation et des tendances épidémiologiques dans une région qui bénéficiait en permanence de mesures de lutte spécifiques, afin de disposer d'une base scientifique pour modifier, le cas échéant, les méthodes utilisées jusqu'alors. On se proposait en outre d'établir dans quelle mesure un traitement suffisant pouvait être assuré à tous les malades excréteurs de bacilles, qu'il s'agisse de cas récents, de patients atteints de rechute ou de tuberculeux chroniques. Enfin l'enquête devait tenter de définir les groupes de population les plus exposés au risque de tuberculose évolutive. On n'a pu tabler sur une variable extrêmement sensible — l'incidence de l'infection tuberculeuse chez les enfants et les jeunes adultes — la vaccination de masse par le BCG, en vigueur en Tchécoslovaquie depuis 1949, ayant été mise en œuvre sans interruption dans le district de Kolín.

Au début de l'enquête, en 1960, on a procédé à un contrôle, basé sur des examens radiologiques et bactériologiques, de toutes les personnes atteintes de tuberculose pulmonaire évolutive ou non évolutive ou porteuses de lésions fibreuses. Au cours de la 1re année (1961) et de la 3e année (1963), toutes les personnes âgées de plus de 14 ans ont fait l'objet d'un examen radiophotographique, la participation de la population atteignant 95%. Par la suite, les signes d'évolution ont été activement recherchés chez les sujets atteints de tuberculose non évolutive ou porteurs de lésions fibreuses par des examens radiologiques et bactériologiques effectués à intervalles réguliers. Quant aux personnes chez lesquelles tous les examens antérieurs taient négatifs, elles n'ont fait l'objet d'investigations que lorsque des symptômes les amenaient à consulter.

En 1961, on a pratiqué des épreuves tuberculiniques chez 90% des habitants âgés de plus de six ans, et soumis un tiers environ de la population à de nouveaux tests en 1963. Toutes les personnes reconnues atteintes de tuberculose évolutive ont été mises en traitement ambulatoire de longue durée après un bref séjour à l'hôpital. La vaccination obligatoire par le BCG a été appliquée aux nouveau-nés et des revaccinations ont été effectuées chez les sujets de 14 et 19 ans présentant une réaction tuberculinique négative.

Les données ci-après ont été recueillies durant les quatre premières années (1961-1964) du déroulement de l'enquête.

L'analyse des réactions tuberculiniques chez les enfants et les jeunes adultes a montré que l'allergie conférée par le BCG tchécoslovaque était faible comparée à celle suscitée par le vaccin danois utilisé en 1949. Un fort pourcentage des habitants non vaccinés âgés de plus de 35 ans avaient été antérieurement en contact avec des bacilles tuberculeux virulents. Dans les groupes

d âge supérieur, chez les personnes à image radiologique normale comme chez les porteurs de calcifications pulmonaires ou les sujets atteints de tuberculose avérée, la proportion des non-réacteurs était en légère augmentation.

On a apprécié la situation épidémiologique au début et au cours de l'enquête en se basant sur le nombre de nouveaux cas de tuberculose ouverte, le nombre de rechutes et la prévalence de la tuberculose évolutive.

Durant la période 1961-1964, 241 nouveaux cas de tuberculose bactériologiquement confirmés ont été découverts chez des personnes qui présentaient antérieurement des images radiologiques normales, et 107 chez des sujets classés comme porteurs de lésions pulmonaires fibreuses. Le plus grand nombre de cas (128, soit 43%) a été diagnostiqué à l'occasion des examens radiophotographiques de masse de 1961 et 1963; 30% des cas ont été dépistés chez des sujets porteurs de lésions fibreuses, 19% chez des malades présentant des symptômes pulmonaires, et 8% par d'autres méthodes d'examen. Cependant, si l'on tient compte uniquement des formes les plus graves — avec présence de bacilles à l'examen microscopique direct — on remarque que des coefficients de dépistage différents ont été obtenus suivant les méthodes. Sur 102 personnes appartenant à ce groupe, 41 (40%) étaient porteuses de lésions fibreuses avant que le diagnostic de tuberculose ne soit posé; 25 (24%) avaient consulté pour des symptômes pulmonaires; 23 (23%) avaient été dépistées par radiophotographie de masse et chez 13 (13%) le diagnostic avait été porté par d'autres méthodes.

Au cours de la même période, des rechutes de tuberculose confirmées bactériologiquement ont été observées chez 80 malades classés dans la catégorie « tuberculose non évolutive », soit une incidence annuelle de 1,6%, avec une fréquence relativement élevée chez les sujets insuffisamment traités avant le début de l'enquête. Fait intéressant, chez 30% des malades atteints de rechute, les bacilles tuberculeux ont été décelés par la microscopie directe, bien que l'on ait procédé chez les sujets souffrant de tuberculose non évolutive à des examens radiologiques et bactériologiques réguliers.

La prévalence de la tuberculose pulmonaire ouverte a été calculée en recensant chaque année les malades qui avaient excrété des bacilles et étaient en vie au 31 décembre. Dans ce groupe, on trouvait notamment les nouveaux cas de tuberculose ouverte, les malades atteints de rechute et les excréteurs chroniques de bacilles. L'analyse de ces données, pendant la période 1960-1964, montre qu'un accroissement de la prévalence ne s'est manifesté qu'à une seule occasion, de 1960 à 1961, à la suite de la première campagne de dépistage de masse de 1961. Dès 1962, on a noté un déclin continu et relativement rapide de la prévalence, qui s'est maintenu en 1963 et 1964 malgré la répétition des opérations de dépistage en 1963. Le nombre total des malades excrétant des bacilles est passé de 150 en 1960 à 91 en 1964, soit une diminution de 39%. Cette baisse a été plus nette encore dans le groupe des malades positifs à l'examen microscopique direct, dont le nombre est passé de 80 en 1960 à 34 en 1964 (−57%). Cette chute de la prévalence de la tuberculose ouverte doit être attribuée en grande partie à la réduction du nombre des malades chroniques. En revanche, le nombre des cas de tuberculose ouverte récemment découverts et positifs à l'examen microscopique direct n'a diminué que dans une faible proportion.

Il importe de souligner que durant les quatre premières années de l'enquête, la répétition des examens radiophotographiques de masse n'a pas eu d'influence nette sur le dépistage des nouveaux cas de tuberculose ouverte à bacilloscopie positive. Durant cette période, 23 malades de ce genre, en moyenne, ont été découverts chaque année, que l'on ait procédé ou non à de tels examens.

La prévalence de la tuberculose pulmonaire non évolutive a été en augmentation de 34% entre 1960 et 1964, ce qui est considéré comme une preuve de l'efficacité des mesures de lutte antituberculeuse.

Le traitement des malades atteints de lésions ouvertes a permis d'obtenir une proportion de négativations de 100% dans les cas récents, de 98% en cas de rechute et de 70% chez les malades chroniques. Ces résultats favorables se maintenaient après six ans.

Au début des investigations, on comptait 53 tuberculeux chroniques par 100 000 habitants; quatre ans plus tard, cette proportion s'était abaissée à 8, soit un gain de 85%, dû à la négativation de l'expectoration chez des malades chroniques, aux décès de malades porteurs de bacilles résistants et au traitement systématique des nouveaux cas et des rechutes.

Une résistance primaire aux médicaments antituberculeux a été décelée dans 4% des cas récemment découverts. Une résistance secondaire est apparue chez environ 25% des malades atteints de rechute et chez la plupart des tuberculeux chroniques. Les sujets excrétant au moins une fois par an des bacilles résistant à un ou plusieurs médicaments étaient au nombre de 60 par 100 000 habitants en 1961 et de 14 en 1964.

Le risque d'apparition de tuberculose ouverte a été évalué, en fonction de l'âge et du sexe, parmi les personnes présentant des altérations de l'image radiologique et les personnes à image pulmonaire normale. Chez les sujets atteints de tuberculose non évolutive, des lésions ouvertes sont apparues avec une fréquence annuelle de 1,3%, le taux correspondant étant de 0,8% chez les porteurs de lésions fibreuses et de 0,08% chez les personnes ne présentant aucune lésion à l'examen radiologique.

Les résultats de l'enquête de Kolín montrent que la lutte antituberculeuse doit tenir compte de certaines priorités: traitement convenable de tous les malades atteints de tuberculose évolutive et diagnostic précoce des nouveaux cas. La vaccination de masse par le BCG et le dépistage de masse par radiophotographie doivent être utilisés avec discernement et réservés surtout aux groupes particulièrement exposés.

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Annex 1

CLASSIFICATION CODE FOR PHOTOFLUOROGRAPHIC FINDINGS

FIRST DIGIT: DESCRIPTION OF TYPE OF LESIONS

0 = no pathological findings
1 = other pathological findings (not mentioned below)
2 = cardiac or intra-thoracic vascular pathology
3 = isolated pleural adhesion or closed costophrenic angle
4 = calcified parenchymal spot, and/or calcium in hilus
5 = pleurisy, including sequelae not mentioned above
6 = sequelae of thoracic surgery
7 = pulmonary infiltration—no definite cavity
8 = pulmonary infiltration—definite cavity
9 = not done, or technically inadequate

If more than one type of lesion is present, the lesion having the highest code number is recorded.

SECOND DIGIT: LOCALIZATION OF LESIONS TYPE 5-8

0 = not applicable (not coded as 5-8 in first digit)
1 = right upper, or right upper and lower
2 = left upper, or left upper and lower
3 = 1 + 2
4 = 1 + left lower
5 = 2 + right lower
6 = right lower
7 = left lower
8 = 6 + 7

The division between upper and lower zones of the lung field is by a horizontal line through the lower edge of the anterior part of the third rib.

THIRD DIGIT: TOTAL SIZE OF LESIONS TYPE 5-8

0 = not applicable (not coded as 5-8 in first digit)
1 = one or more pin-point lesion(s)
2 = multiple miliary lesions
3 = not more than circle with diameter half intercostal width
4 = not more than circle with diameter one intercostal width
5 = not more than circle with diameter two intercostal width
6 = not more than one-third of a lung
7 = not more than two-thirds of a lung
8 = not more than one lung
9 = more than one lung

The unit of measurement is the average width of the posterior fifth to seventh intercostal space, just lateral of the hilus shadows.

Annex 2

BACTERIOLOGICAL EXAMINATION

COLLECTION OF MATERIAL

For in-patients, bacteriological examination of the morning sputum was carried out. If the amount of sputum was less than 1 ml, a 24-hour specimen was investigated. A voluntary expectoration technique was used for out-patients. Laryngeal swabbing was carried out after the sputum specimen had been obtained. Every person to be examined had three laryngeal swabs taken at a single sitting.

DIRECT MICROSCOPY

Smears for microscopic examination were stained by the Ziehl-Neelsen method. At least 50 randomly selected fields were scrutinized in each slide.

Results of microscopic examination were classified as follows: (0) no acid-fast bacilli found, (1) occasional—up to 20, (2) numerous—21 to 100, (3) many bacilli—more than 100.

CULTURES

Strains were isolated in liquid Šula medium and on solid Löwenstein-Jensen medium. One investigation (carried out on sputum specimen, series of 3 laryngeal swabs, urine, etc) consisted in inoculating material into 4 liquid and on 2 solid media. Cultures were read after 6 and 9 weeks of incubation.

Classification of culture findings was as follows: (0) no growth, (1) up to 20 colonies, (2) 21-100 colonies, (3) more than 100 colonies, (4) contaminated.

BIOLOGICAL TESTING

For all patients in whom tubercle bacilli were isolated, a biological test was carried out on guinea-pigs. If bovine tuberculosis was suspected, a virulence test was also carried out on rabbits; and if the presence of atypical mycobacteria was suspected, on white mice.

DRUG-SENSITIVITY TESTS

Tests of sensitivity to isoniazid, streptomycin and PAS were carried out for all strains of *Myco. tuberculosis* isolated; sensitivity tests to the minor drugs were carried out only where these drugs were used for treatment. Sensitivity tests were done in liquid and on solid media containing the drug concentrations listed in the tabulation below:

Anti-tuberculosis drug	*Concentration of antituberculosis drug in the culture medium (μg/ml)*	
	Šula liquid medium	*Löwenstein-Jensen solid medium*
Isoniazid	0.2- 1-10	0.2- 1-10
Streptomycin	1 - 3-10	1 - 3-10
PAS	1 - 3-10	1 - 3-10
Ethionamide	2 - 5-10	10 -20-40
Pyrazinamide	4 - 8-16	—
Viomycin	2 -10-20	10 -20-40
Cycloserine	—	12.5-25-50
Conteben	—	0.5- 1- 2.5

Sensitivity tests were as a rule performed with 8-day-old subcultures from liquid media, only exceptionally with primary cultures. Evaluation was done after 3 weeks, using the same scale as for culture investigation. If the control culture did not grow well within this period, incubation was continued for another week.

Growth in the drug-containing medium was compared with growth in the control medium, and the drug-sensitivity evaluated by the criteria below:

No. of colonies in control medium	*No. of colonies in medium with drug*	*Drug-sensitivity assigned to strain*
100+	11+	Resistant
100+	0-10	Sensitive
21-100	11+	Resistant
21-100	0-10	Sensitive
15-20	3+	Resistant
15-20	1-2	Doubtful *

* The investigation was repeated.

Annex 3

CLASSIFICATION OF TUBERCULOSIS

PULMONARY TUBERCULOSIS (P)

Active disease

P I-A. *Bacillary tuberculosis.* Cases of pulmonary tuberculosis found to be excreting tubercle bacilli by bacteriological examination (direct microscopy, culture or biological investigation) at least once during the past 12 months.

P II-A. *Bacteriologically quiescent tuberculosis.* Cases of previous bacillary tuberculosis in which bacteriological examinations had remained negative over a period of 12 months.

Should further bacteriological examinations remain negative, the cases are kept in this group for 24 months if there was evidence of cavitation at the time of diagnosis of active tuberculosis, or for 12 months if there was no evidence of cavitation. They are then transferred to the inactive group, P III-A.

Should tubercle bacilli be found in the sputum of a person assigned to group P II-A, he or she is transferred back to P I-A.

P I-B. *Active non-bacillary tuberculosis.* Cases with negative bacteriological findings, where the diagnosis of active tuberculosis of the respiratory system was established on the basis of:

(*a*) radiographic evidence (on at least 2 films taken at 3-month intervals) supported by a positive tuberculin test, or

(*b*) histological investigation of tissue from the respiratory tract.

Persons whose disease runs a favourable course are kept in this group for 2 years and then transferred to the inactive group.

Should persons assigned to the active non-bacillary tuberculosis group be found to be excreting tubercle bacilli, they are transferred to group P I-A.

Inactive disease

P III-A. *Inactive tuberculosis previously confirmed bacteriologically or histologically.* Cases without photofluorographic or bacteriological evidence of activity, after discharge from group P II-A, or from P I-B if the diagnosis of tuberculosis was previously confirmed histologically.

P III-B. *Inactive tuberculosis not previously confirmed either bacteriologically or histologically.* Cases without photofluorographic or bacteriological evidence of activity after discharge from group P I-B if the diagnosis of tuberculosis was never confirmed histologically.

Should a bacteriological examination of a person in group P III-A or group P III-B show the presence of tubercle bacilli, the case is transferred to group P I-A as a relapse. Similarly, should a person in group P III-A or P III-B show evidence of radiographic progression with negative bacteriological findings, and another etiology of the disease should be improbable, the case is transferred to group P I-B as a relapse.

Persons with no evidence of activity remain in the group P III-A or P III-B for the rest of their life.

P IV. *Fibrotic lesions in the lungs.* All persons with fibrotic lesions in the lungs, in all probability of tuberculous origin, detected mostly by photofluorography without any bacteriological, photofluorographic or clinical signs of activity, for whom tuberculosis of the respiratory system was never diagnosed previously.

Persons registered in this group remain there for the rest of their life, unless the diagnosis of active tuberculosis is established or the lesion is found to be non-tuberculous.

EXTRAPULMONARY TUBERCULOSIS (EP)

These groups, in which the letter P is replaced by EP, correspond to the groups defined above, with the differences that the disease involved is extrapulmonary and that there is no group EP IV.

APPENDIX TABLE 1

TUBERCULOSIS MORTALITY AND MORBIDITY DATA FOR CZECHOSLOVAKIA, 1954, 1957 1960 AND 1963

	1954		1957		1960		1963	
	No.	Rate [a]	No.	Rate [a]	No.	Rate [a]	No.	Rate [a]
Tuberculosis mortality: all types	6 321	48.8	4 938	37.0	3 435	25.2	2 654	19.0
children up to 15 years	284	8.1	91	2.5	29	0.8	8	0.2
Prevalence of notified pulmonary bacillary tuberculosis:								
all ages	25 464	195.5	27 249	211.1	15 971	116.6	11 467	81.9
children up to 15 years	208	5.9	181	4.9	64	1.7	79	2.1
New cases of pulmonary tuberculosis and relapses:								
all ages	23 726	183.2	26 871	201.2	23 280	170.5	17 810	127.7
children up to 15 years	3 222	91.4	2 990	80.7	1 561	42.0	744	20.4
Incidence of tuberculosis meningitis in children up to 15 years	310	8.8	126	3.4	31	0.8	15	0.4

[a] Per 100 000 population.

APPENDIX TABLE 2

MEDICAL FACILITIES IN TUBERCULOSIS DEPARTMENTS IN CZECHOSLOVAKIA IN 1954, 1957, 1960 AND 1963

	1954		1957		1960		1963	
	No.	Rate [a]	No.	Rate [a]	No.	Rate [a]	No.	Rate [a]
No. of tuberculosis departments in polyclinics	385	3.0	362	2.7	358	2.6	358	2.6
No. of specialists	705	5.4	833	6.2	1 025	7.5	940	6.7
No. of beds	17 085	131.9	18 [illegible]	138.6	20 223	148.1	19 177	137.5
No. of photofluorograms	1 573 659	12 150	1 812 473	13 568	3 547 884	52 984	4 608 074	32 906
No. of specimens investigated microbiologically for tubercle bacilli	408 471 [b]	5 343	728 675 [b]	7 811	1 048 950	7 682	1 036 506	7402

[a] Rates per 100 000 population.

[b] In Bohemia and Moravia only (9 329 036 inhabitants).

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APPENDIX TABLE 3

NUMBER OF INHABITANTS OF CZECHOSLOVAKIA (ON 1 JULY 1961) AND OF KOLÍN DISTRICT (ON 1 MARCH 1961, ACCORDING TO CENSUS)

Age-group (years)	Czechoslovakia			Kolín district		
	Male	Female	Total	Male	Female	Total
0-14	1 904 934	1 822 952	3 727 886	11 463	10 927	22 390
15-24	997 884	971 857	1 969 741	6 492	6 239	12 731
25-34	924 953	931 041	1 855 994	6 097	6 271	12 368
35-44	[illegible]	871 894	1 695 459	5 419	5 704	11 123
45-54	[illegible]	916 021	1 784 454	7 043	7 728	14 771
55-64	707 384	813 542	1 520 926	6 511	7 521	14 032
65-74	344 494	494 924	839 418	3 565	5 062	8 627
75+	146 174	235 941	382 115	1 608	2 768	4 376
Total	6 721 821	7 058 172	13 779 993	48 198	52 220	100 418

APPENDIX TABLE 4

PARTICIPATION OF THE POPULATION OF KOLÍN DISTRICT IN THE FIRST MASS TUBERCULIN TESTING IN 1961

Age-group (years)	No. of [illegible]		No. of tests		No. of tests read		Percentage of population tested		Percentage of population with tests read		Percentage of tests read in tested population	
	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females	Males	Females
7-14	[illegible]	[illegible]	[illegible]	6 039	[illegible]	5 926	98.16	98.35	96.22	96.62	98.03	98.24
15-24	6 246	[illegible]	[illegible]	5 93[illegible]	[illegible]	5 041	33.94	93.95	76.26	89.33	90.84	95.08
25-44	11 221	[illegible]	10 645	11 38[illegible]	[illegible]	11 023	94.87	97.01	89.16	93.97	93.99	96.87
45-64	13 050	[illegible]	12 543	14 22[illegible]	[illegible]	[illegible]	86.11	96.96	91.85	94.94	95.57	97.92
65+	[illegible]	7 [illegible]	[illegible]	6 192	[illegible]	5 539	89.69	79.28	85.29	76.04	95.10	95.91
Total	42 079	46 660	39 348	43 762	37 323	42 459	93.51	93.79	88.70	91.00	94.85	97.02

[a] Children who attained 6 years of age in 1961 but did not attend school until 1 September 1961 are not included.

APPENDIX TABLE 5

SIZE DISTRIBUTION OF REACTIONS TO MANTOUX 2 TU TESTS IN PERSONS AGED 7, 11, 15, 19 AND 24 YEARS IN KOLIN DISTRICT IN 1961

Diameter of reaction (mm)	7 years			11 years			15 years			19 years			24 years		
	Total	Vaccinated [a]	Unvaccinated	Total	Vaccinated [b]	Unvaccinated	Total	Vaccinated [b]	Unvaccinated	Total	Vaccinated [b]	Unvaccinated	Total	Vaccinated [b]	Unvaccinated
0-1	603	464	33	690	559	118	181	90	15	50	26	7	24	18	1
2-3	494	442	8	751	659	44	90	48	10	27	12	—	27	17	1
4-5	117	118	1	760	644	16	61	3	1	53	43	2	23	13	—
6-7	80	80	3	95	85	9	129	86	4	56	23	4	28	16	1
8-9	49	49	—	53	39	8	112	110	6	61	41	3	38	26	3
10-11	30	24	1	47	31	6	173	121	8	117	89	4	72	44	5
12-13	38	34	1	69	44	9	192	149	8	124	89	7	90	53	14
14-15	38	35	—	64	29	12	181	124	4	184	136	19	126	78	17
16-17	60	54	1	69	35	15	181	121	15	154	97	21	127	64	32
18-19	42	23	5	56	27	12	148	99	3	109	56	28	125	59	32
20-21	21	17	—	43	14	21	87	56	9	83	40	29	93	31	26
22-23	7	6	—	16	7	5	40	27	5	50	23	18	62	22	25
24-25	5	5	—	8	4	4	25	17	7	14	6	7	25	4	12
26-27	—	—	—	3	1	2	8	6	1	9	3	4	7	1	4
28-29	—	—	—	—	—	—	3	3	—	3	—	2	3	1	1
30-31	1	—	—	—	—	—	2	2	—	—	—	—	2	1	1
32 +	—	—	—	—	—	—	—	—	—	1	—	1	1	—	1
Total [c]	1 459	1 211	66	1 540	898	281	1 653	1 092	117	1 055	664	156	873	441	176

[a] With Czech vaccine.

[b] With Danish vaccine.

[c] The difference between the total number of persons under review and the sum total of vaccinated and unvaccinated persons is made up by persons for whom no accurate data on previous BCG vaccination are available.

APPENDIX TABLE 6 A

SIZE DISTRIBUTION OF REACTIONS TO MANTOUX 2 TU TESTS IN PERSONS IN KOLÍN DISTRICT WITH NORMAL PHOTOFLUOROGRAMS

Diameter of induration (mm)	Male						Female					
	25-44 years		45-64 years		65 + years		25-44 years		45-64 years		65 + years	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-1	310	3.8	420	4.9	227	12.1	498	5.4	622	6.2	321	10.4
2-3	145	1.8	160	1.9	81	4.3	473	5.1	570	5.7	204	6.6
4-5	107	1.3	127	1.5	54	2.9	345	3.7	469	4.7	210	6.8
6-7	106	1.3	201	2.4	129	6.8	287	3.1	450	4.5	302	9.8
8-9	157	1.9	266	3.1	93	4.9	237	2.6	326	3.3	181	5.8
10-11	323	3.9	485	5.7	168	8.9	353	3.8	403	4.0	164	5.3
12-13	695	8.4	833	9.7	185	9.8	625	6.7	646	6.5	175	5.6
14-15	1 198	14.5	1 326	15.5	210	11.1	926	10.0	1 048	10.5	254	8.2
16-17	1 489	18.1	1 535	18.0	246	13.1	1 109	12.0	1 136	11.4	245	7.9
18-19	1 518	18.4	1 341	15.7	202	10.7	1 337	14.4	1 261	12.6	282	9.1
20-21	1 197	14.5	962	11.3	162	8.6	1 255	13.5	1 276	12.8	261	8.4
22-23	589	7.1	528	6.2	81	4.3	867	9.4	840	8.4	213	6.9
24-25	272	3.3	245	2.9	26	1.4	568	6.1	525	5.2	144	4.6
26-27	88	1.1	71	0.8	17	0.9	224	2.4	233	2.3	73	2.4
28-29	28	0.3	22	0.3	3	0.2	101	1.1	115	1.1	39	1.3
30-31	13	0.2	12	0.1	—	—	40	0.4	54	0.5	16	0.5
32 +	5	0.1	7	0.1	—	—	25	0.3	31	0.3	14	0.4
Total	8 240	100	8 541	100	1 884	100	9 270	100	10 005	100	3 098	100
Estimated percentage of positive reactions [a]	92.0		89.7		69.7		82.0		78.3		62.8	
Mean diameter of positive reactions [a]	17.4 ± 3.88		16.7 ± 4.09		16.1 ± 4.24		18.3 ± 4.60		18.1 ± 4.80		17.9 ± 5.41	

[a] Estimated on the assumption that the reactions have a truncated normal distribution, with the point of truncation at 12 mm.

APPENDIX TABLE 6 B

SIZE DISTRIBUTION OF REACTIONS TO MANTOUX 2 TU TESTS IN PERSONS IN KOLÍN DISTRICT WITH CALCIFICATIONS IN THE LUNGS

Diameter of induration (mm)	Male						Female					
	25-44 years		45-64 years		65 + years		25-44 years		45-64 years		65 + years	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-1	2	0.4	33	3.5	25	7.3	11	1.7	78	6.8	56	12.8
2-3	3	0.5	10	1.1	10	2.9	14	2.1	62	5.4	34	7.8
4-5	1	0.2	9	0.9	5	1.5	7	1.1	39	3.4	29	6.6
6-7	3	0.5	21	2.2	22	6.4	9	1.4	60	5.2	34	7.8
8-9	5	0.9	30	3.2	16	4.7	14	2.1	50	4.3	17	3.9
10-11	6	1.1	47	4.9	25	7.3	19	2.9	48	4.2	19	4.3
12-13	36	6.6	87	9.1	37	10.8	28	4.2	74	6.4	21	4.8
14-15	68	12.4	127	13.3	47	13.7	63	9.5	95	8.3	30	6.8
16-17	108	19.7	202	21.1	52	15.2	73	11.0	137	11.9	42	9.6
18-19	123	22.4	150	15.8	40	11.7	105	15.8	148	12.9	42	9.6
20-21	103	18.8	118	12.4	31	9.1	119	17.9	136	11.8	34	7.8
22-23	51	9.3	61	6.4	22	6.4	102	15.4	101	8.8	32	7.3
24-25	23	4.2	35	3.7	5	1.5	48	7.2	57	5.0	26	5.9
26-27	12	2.2	10	1.1	4	1.2	29	4.4	37	3.2	14	3.2
28-29	4	0.7	5	0.6	1	0.3	7	1.1	15	1.3	4	0.9
30-31	—	—	1	0.5	1	0.3	9	1.4	8	0.7	4	0.9
32 +	—	—	1	0.1	—	—	7	1.1	6	0.5	1	0.2
Total	548	100	951	100	343	100	664	100	1 151	100	439	100
Estimated percentage of positive reactions[a]	99.8		93.5		83.4		92.2		77.4		62.2	
Mean diameter of positive reactions[a]	18.3 ± 3.67		17.0 ± 4.28		16.0 ± 4.50		19.6 ± 4.53		18.3 ± 4.99		18.6 ± 5.14	

[a] Estimated on the assumption that the reactions have a truncated normal distribution, with the point of truncation at 12 mm.

APPENDIX TABLE 6 C

SIZE DISTRIBUTION OF REACTIONS TO MANTOUX 2 TU TESTS IN PERSONS IN KOLÍN DISTRICT WITH BACTERIOLOGICALLY CONFIRMED PULMONARY TUBERCULOSIS

Diameter of induration (mm)	Male						Female					
	25-44 years		45-64 years		65 + years		25-44 years		45-64 years		65 + years	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0-1	—	—	10	3.4	5	5.4	2	1.3	6	4.8	2	4.3
2-3	1	0.6	—	—	1	1.1	—	—	1	0.8	—	—
4-5	—	—	1	0.3	1	1.1	1	0.7	4	3.2	1	2.1
6-7	1	0.6	2	0.7	1	1.1	—	—	2	1.6	1	2.1
8-9	1	0.6	7	2.4	3	3.3	3	2.0	3	2.4	4	8.5
10-11	1	0.6	9	3.1	3	3.3	4	2.6	1	0.8	2	4.3
12-13	13	7.5	23	8.0	5	5.4	4	2.6	2	1.6	2	4.3
14-15	22	12.6	35	12.1	10	10.9	9	5.9	10	7.9	5	10.6
16-17	25	14.4	46	15.9	16	17.4	11	7.2	11	8.7	9	19.2
18-19	47	27.0	57	19.7	19	20.6	32	21.1	25	19.8	6	12.8
20-21	33	19.0	44	15.2	10	10.9	26	17.1	23	18.3	4	8.5
22-23	13	7.5	32	11.0	7	7.6	27	17.8	15	11.9	5	10.6
24-25	10	5.7	14	4.8	9	9.8	17	11.2	12	9.5	1	2.1
26-27	4	2.3	7	2.4	2	2.2	8	5.3	7	5.6	4	8.5
28-29	1	0.6	1	0.3	—	—	3	2.0	2	1.6	—	—
30-31	1	0.6	1	0.3	—	—	3	2.0	2	1.6	1	2.1
32 +	1	0.6	1	0.3	—	—	2	1.3	—	—	—	—
Total	174	100	290	100	92	100	152	100	126	100	47	100
Estimated percentage of positive reactions [a]	100.0		93.8		88.0		94.7		87.8		85.1	
Mean diameter of positive reactions [a]	18.2 ± 4.10		18.0 ± 4.22		17.4 ± 3.41		20.7 ± 4.20		20.2 ± 3.99		17.6 ± 5.61	

[a] Estimated on the assumption that the reactions have a truncated normal distribution, with the point of truncation at 12 mm.

APPENDIX TABLE 7

PREVALENCE OF PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, BY SEX, AGE AND TYPE OF DISEASE [a]

Age (years)	Male										Female									
	P I-A		P II-A		P I-B		Total active		P III-A P III-B		P I-A		P II-A		P I-B		Total active		P III-A P III-B	
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	Rate
1960																				
0-14	—	—	—	—	2	17	2	17	10	87	2	18	—	—	4	37	6	55	7	64
15-24	1	16	5	77	3	46	9	139	26	400	2	32	2	32	4	64	8	128	33	529
25-44	23	200	25	217	17	147	65	564	234	2 031	12	100	13	108	16	134	41	342	222	1 854
45-64	65	480	58	428	22	162	145	1 070	281	2 073	16	105	22	144	10	66	48	315	169	1 109
65 +	21	406	30	580	13	251	64	1 237	93	1 798	8	102	17	217	8	102	33	421	72	920
Total	110	228	118	245	57	118	285	591	644	1 336	40	77	54	103	42	80	136	260	503	963
1961																				
0-14	—	—	—	—	1	9	1	9	9	79	—	—	1	9	1	9	2	18	7	63
15-24	3	46	3	46	4	62	10	154	25	385	5	80	1	16	5	80	11	176	34	545
25-44	28	243	25	217	19	165	72	625	248	2 154	18	150	9	75	18	150	45	376	238	1 987
45-64	86	634	44	325	22	162	152	1 121	309	2 280	23	151	17	111	6	39	46	302	179	1 174
65 +	40	773	20	387	6	116	66	1 276	120	2 319	30	383	9	115	10	128	49	626	89	1 137
Total	157	326	92	191	52	108	301	625	711	1 475	76	146	37	71	40	77	153	293	547	1 048
1962																				
0-14	1	9	—	—	2	17	3	26	6	52	—	—	—	—	2	18	2	18	9	82
15-24	2	31	4	62	3	46	9	139	24	370	1	16	4	64	5	80	10	160	28	449
25-44	22	191	30	261	14	122	66	573	261	2 266	7	58	18	150	12	100	37	309	257	2 146
45-64	44	325	70	516	21	155	135	996	319	2 354	13	85	15	98	5	33	33	216	169	1 239
65 +	25	483	31	599	7	135	63	1 218	134	2 590	23	294	27	345	9	115	59	754	98	1 252
Total	94	195	135	280	47	98	276	573	744	1 544	44	84	64	123	33	63	141	270	581	1 113
1963																				
0-14	—	—	1	10	4	40	5	50	6	60	—	—	—	—	2	21	2	21	9	96
15-24	—	—	3	40	1	13	4	54	25	335	1	14	3	42	2	28	6	84	31	433
25-44	21	174	26	216	7	58	54	448	281	2 333	4	32	16	129	5	40	25	201	274	2 206
45-64	43	339	64	505	12	95	119	938	343	2 704	6	43	7	50	3	21	16	114	194	1 354
65 +	26	452	33	573	5	87	64	1 112	152	2 671	25	263	28	317	4	45	57	646	133	1 507
Total	90	188	127	265	29	61	246	514	807	1 686	36	69	54	104	16	31	106	205	641	1 237
1964																				
0-14	—	—	—	—	1	9	1	9	7	66	1	10	—	—	1	10	2	20	8	80
15-24	2	27	1	13	1	13	4	54	28	377	2	28	1	14	2	28	5	70	32	451
25-44	9	75	24	200	7	58	40	333	279	2 324	1	8	6	48	10	80	17	137	277	2 227
45-64	34	272	40	320	13	104	87	696	371	2 969	4	29	9	65	3	22	16	115	192	1 378
65 +	20	373	25	466	4	75	49	914	183	3 412	18	216	20	240	3	36	41	492	156	1 872
Total	65	135	90	188	26	54	181	378	868	1 813	26	51	36	70	19	37	81	158	665	1 284

[a] Rates are per 100 000. The disease classification used is explained briefly below.

Active tuberculosis

P I-A Bacillary tuberculosis
P II-A Bacteriologically quiescent tuberculosis
P I-B Non-bacillary tuberculosis

Inactive tuberculosis

P III-A Inactive tuberculosis previously confirmed bacteriologically or histologically.
P III-B Inactive tuberculosis not previously confirmed bacteriologically or histologically

For further details, see Annex 3.

APPENDIX TABLE 8

PREVALENCE OF BACILLARY PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT ON 31 DECEMBER FROM 1960 TO 1964, BY MODE OF FINDING OF TUBERCLE BACILLI

	1960				1961				1962				1963				1964			
	Male		Female		Male		Female		Male		Female		Male		Female		Male		Female	
	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy	Total	By microscopy
Newly discovered case previously with																				
normal X-ray	22	12	13	7	71	12	44	8	21	8	13	8	36	9	21	3	16	8	8	3
fibrotic lesions	7	2	4	—	11	5	6	2	14	5	13	3	24	11	7	3	15	5	8	2
Subtotal	29	14	17	7	82	17	50	10	35	13	26	11	60	20	28	6	31	13	16	5
Relapses	22	9	7	1	18	8	7	—	17	8	1	1	9	4	4	1	12	5	4	—
Chronic bacillary excretors	41	35	8	7	31	15	9	4	15	6	2	—	10	6	1	—	8	5	—	—
Remainder	18	6	8	1	26	12	10	2	27	8	15	3	11	5	3	1	14	5	6	1
Total	110	64	40	16	157	52	76	16	94	35	44	15	90	35	36	8	65	28	26	6

APPENDIX TABLE 9

ANNUAL FREQUENCY OF ACTIVE PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64 BY SEX, AGE AND TYPE OF DISEASE[a]

Age-group (years)	Bacillary tuberculosis									Active non-bacillary tuberculosis								
	1961		1962		1963		1964		1961-64	1961		1962		1963		1964		1961-64
	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.	No.	Rate	No.	Rate	No.	Rate	No.	Rate	No.
Male																		
0-14	—	—	1	9	—	—	—	—	1	—	—	1	9	2	20	—	—	3
15-24	3	46	2	31	—	—	2	27	7	4	62	—	—	1	13	—	—	5
25-44	19	130	9	62	12	100	4	33	40	9	78	2	17	5	42	1	8	17
45-64	41	302	15	111	30	237	15	120	101	17	125	6	44	6	47	6	48	35
65 +	27	522	11	213	20	348	11	200	69	3	58	3	58	3	52	2	37	11
Total	86	178	38	79	62	129	32	67	218	33	68	12	25	17	35	9	19	71
Female																		
0-14	—	—	—	—	—	—	1	10	1	—	—	2	18	1	11	—	—	3
15-24	4	64	—	—	1	14	1	14	6	4	64	2	32	1	14	1	14	8
25-44	7	58	4	33	3	24	—	—	14	11	92	1	8	4	32	3	24	19
45-64	12	79	1	6	2	13	3	22	27	3	20	2	13	2	14	1	7	8
65 +	29	370	11	213	24	272	12	144	82	9	115	4	51	1	11	2	24	16
Total	52	100	16	31	30	58	17	33	130	27	52	11	21	9	17	7	14	54
Grand total	138	138	54	54	92	92	49	47	348	60	60	23	23	26	26	16	16	125

[a] The frequency rate is given per 100 000.

APPENDIX TABLE 10

INCIDENCE OF BACILLARY PULMONARY TUBERCULOSIS IN KOLIN DISTRICT IN 1961-64, BY MODE OF DETECTION[a]

Mode of detection	Incidence				Total	
	1961	1962	1963	1964	No.	Percentage of microscopically positive cases
Previously normal chest X-rays						
On account of symptoms	[illegible] (8)	16 (6)	16 (4)	17 (7)	66 (25)	38
By mass photofluorography	97 (11)	10 (4)	41 (8)	—	148 (23)	16
By other preventive examination	5 (1)	11 (7)	4 (1)	7 (4)	27 (13)	(48)
Total	119 (20)	37 (17)	61 (13)	24 (11)	241 (61)	25
Previous fibrotic lung lesions						
All methods	19 (7)	29 (9)	34 (16)	25 (9)	107 (41)	38
Grand Total	138 (27)	66 (26)	95 (29)	49 (20)	348 (102)	29

[a] The number of persons found to be excreting mycobacteria on direct smear microscopy is given in parentheses.

APPENDIX TABLE 11

ESTIMATED ANNUAL INCIDENCE OF PULMONARY BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT (FOR 1962 AND 1963) IN PERSONS WITH PREVIOUSLY NORMAL CHEST X-RAYS

Age-group (years)	Male		Female		Total	
	No.	Rate[a]	No.	Rate[a]	No.	Rate[a]
0-14	1	5	—	—	1	3
[illegible]	[illegible]	[illegible]	1	[illegible]	2	[illegible]
[illegible]-44	[illegible]	[illegible]	4	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	6	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	25	[illegible]	[illegible]	[illegible]
Total	[illegible]	[illegible]	36	[illegible]	[illegible]	[illegible]

[a] In this table only, the rates are given per 100 000 persons with normal photofluorographic findings (i.e., excluding cases of tuberculosis and fibrotic lesions). The numbers of cases are given for 2 years (1962 and 1963), while the rates are annual rates.

APPENDIX TABLE 12

COMPARISON OF THE NUMBER OF NEWLY DISCOVERED CASES OF BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64 WITH THE EXPECTED INCIDENCE OF TUBERCULOSIS

Year	New cases of bacillary tuberculosis discovered			Expected incidence of bacillary tuberculosis	Difference between No. of cases discovered and expected incidence
	on account of symptoms	by photofluorography[a]	Total		
1961	17	102	119	48	+71
1962	16	21	37	43	−6
1963	16	45	61	39	+22
1964	17	7	24	35	−11
Total	66	175	241	165	+76

[a] Including mass photofluorography of the population above 14 years of age, examination of contacts and of selected population groups.

APPENDIX TABLE 13
RELAPSES OF PULMONARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64

	1961			1962			1963			1964			Total		
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total
Bacteriologically confirmed	21	8	29	19	1	20	10	4	14	13 [a]	4	17	63 [a]	17	80
Not bacteriologically confirmed	2	—	2	3	—	3	—	—	—	3	3	6	8	3	11
Total	23	8	31	22	1	23	10	4	14	16	7	23	71	20	91

[a] Including 1 relapse discovered at necropsy (accidental death).

APPENDIX TABLE 14
TUBERCULOSIS MORTALITY IN KOLÍN DISTRICT IN 1961-64

	1961			1962			1963			1964			Total			Average mortality, 1961-64 [a] (%)
	M	F	Total	M	F	Total	M	F	Total	M	F	Total	M	F	Total	
Pulmonary tuberculosis																
Active: P II-A	18	5	23	19	8	27	9	9	18	8	6	14	54	28	82	13.9
P II-A	4	2	6	3	3	6	8	2	10	8	1	9	23	8	31	4.9
P II-B	—	3	3	3	3	6	2	—	2	—	—	—	5	6	11	4.2
Subtotal	22	10	32	25	14	39	19	11	30	16	7	23	82	42	124	8.3
Inactive: P III-A	9	2	11	12	1	13	16	4	20	12	7	19	49	14	63	1.9
P III-B	5	3	8	5	4	9	5	1	6	5	2	7	20	10	30	1.4
Subtotal	14	5	19	17	5	22	21	5	26	17	9	26	69	24	93	1.7
Total	36	15	51	42	19	61	40	16	56	33	16	49	151	66	217	3.1
Extrapulmonary tuberculosis																
Active	—	2	2	2	3	5	2	2	4	—	3	3	4	10	14	6.1
Inactive	—	2	2	3	1	4	1	6	7	4	2	6	8	11	19	2.5
Total	—	4	4	5	4	9	3	8	11	4	5	9	12	21	33	3.4
Fibrotic lung lesions																
	31	14	45	92	46	138	88	53	141	78	47	125	289	160	449	3.1

[a] Average annual mortality as a percentage of the total number of persons registered in the respective group.

APPENDIX TABLE 15

BACTERIOLOGICAL AND RADIOGRAPHIC CONDITION OF 474 PATIENTS IN KOLÍN DISTRICT WITH BACILLARY TUBERCULOSIS ON ADMISSION TO TREATMENT

Condition on admission to treatment	New cases		Relapses		Chronic bacillary excretors		Total	
	No.	%	No.	%	No.	%[a]	No.	%
Bacteriological								
Positive by direct microscopy and by culture	102	29	30	38	27	(59)	150	34
Positive by culture only	246	71	50	62	19	(41)	315	66
Radiographic								
Minimal	110	32	8	10	2	(4)	120	25
Moderately advanced	191	55	57	71	17	(37)	265	56
Far advanced	47	13	15	19	27	(59)	89	19
Cavitation								
Nil	236	68	46	58	7	(15)	289	61
Unilateral, less than 3 cm diameter	88	25	24	30	18	(39)	130	27
Unilateral, more than 3 cm diameter, or bilateral	24	7	10	12	21	(46)	55	12

[a] The percentages for chronic bacillary excretors are given in parentheses to indicate that not too much reliance should be placed on these figures, as the total number of patients in this group was only 46.

APPENDIX TABLE 16

AVERAGE DURATION OF TREATMENT FOR 451 PERSONS HOSPITALIZED WITH BACILLARY TUBERCULOSIS AND 123 PERSONS WITH ACTIVE NON-BACILLARY TUBERCULOSIS IN KOLÍN DISTRICT IN 1961-64

	No. of patients			Duration of hospital treatment (days)								
				Non-cavitary tuberculosis			Cavitary tuberculosis			Total		
	P I-A[a]	P I-B[a]	Total	P I-A	P I-B	Total	P I-A	P I-B	Total	P I-A	P I-B	Total
New cases	335	115	450	121	100	114	245	172	241	161	104	147
Relapses	71	8	79	176	139	170	246	—	246	208	139	201
Chronic bacillary excretors	45	—	45	212	—	212	390	—	390	366	—	366
All groups	451[b]	123	574	131	103	122	276	172	273	189	107	171

[a] Group P I-A: Bacillary tuberculosis; Group P I-B: Active non-bacillary tuberculosis (see Annex 3).
[b] 31 patients in whom the duration of hospitalization was not evaluated are excluded; for details see p. 841.

APPENDIX TABLE 17

PREVALENCE OF STRAINS OF MYCOBACTERIA RESISTANT TO ISONIAZID, STREPTOMYCIN, PAS OR A COMBINATION OF THESE IN KOLÍN DISTRICT IN 1961-64

Drugs	Prevalence of resistant strains								Total	
	New cases		Relapses		Chronic bacillary excretors		Cases diagnosed in 1960 [a]			
	No.	%	No.	%	No.	%	No.	%	No.	%
Isoniazid	4	1.2	17	23.3	12	28.6	10	32.3	43	9.1
Streptomycin	3	0.9	—	—	1	2.4	—	—	4	0.8
PAS	3	0.9	2	2.7	—	—	—	—	5	1.1
Isoniazid + Streptomycin	1	0.3	—	—	9	21.4	—	—	10	2.1
Isoniazid + PAS	—	—	2	2.7	4	9.5	3	9.7	9	1.9
Streptomycin + PAS	—	—	—	—	—	—	—	—	—	—
Isoniazid + Streptomycin + PAS	2 [b]	0.6	1 [c]	1.4	9	21.4	1	3.2	13	2.7
No. of resistant strains	13	3.9	22	30.1	35	83.3	14	45.2	84	17.8
No. of sensitive strains	314	96.1	51	69.9	7	16.7	17	54.8	389	82.2
Total No. of strains	327	100.0	73	100.0	42	100.0	31	100.0	473	100.0
Sensitivity tests not available	21		7		4		7		39	
No. of patients with bacillary tuberculosis	348		90		46		38		512	

[a] Cases diagnosed in 1960 or earlier and still infectious during early part of 1961.
[b] *Mycobacterium avium* was found in one patient.
[c] Mycobacteria of a not yet identified strain were found in this patient.

APPENDIX TABLE 18

[illegible] OF STRAINS OF MYCOBACTERIA [illegible] TO ANTITUBERCULOSIS [illegible]
IN KOLÍN DISTRICT IN 1961-64

Year	New cases			Relapses			Chronic bacillary excretors			Cases diagnosed in 1960 [a]			Total		
	No. of strains investigated	Resistant strains		No. of strains investigated	Resistant strains		No. of strains investigated	Resistant strains		No. of strains investigated	Resistant strains		No. of strains investigated	Resistant strains	
		No.	%		No.	%		No.	%		No.	%		No.	%
1960 & 1961	—	—	—	—	—	—	31	28	(90.3)	31	14	(45.2)	62	42	67.7
1961 only	129	6	4.7	25	8	(32.0)	8	4	(50.0)	—	—	—	162	18	11.1
1962	59	2	3.4	19	7	(36.8)	2	2	(100.0)	—	—	—	80	11	13.8
1963	92	5	5.4	13	3	(23.1)	1	1	(100.0)	—	—	—	106	9	8.5
1964	47	—	—	16	4	(25.0)	—	—	—	—	—	—	63	4	6.3
Total	327	13	4.0	73	22	30.1	42	35	(83.3)	31	14	(45.2)	473	84	17.8

[a] Cases diagnosed in 1960 or [illegible] cases during early part of 1961.

APPENDIX TABLE 19

FIBROTIC LUNG LESIONS IN KOLÍN DISTRICT ON 31 DECEMBER 1960, 1961 AND 1964

Age-group (years)	1960			1961			1964		
	M	F	Total	M	F	Total	M	F	Total
	No. of persons with fibrotic lung lesions								
0-14	24	24	48	23	21	44	10	14	24
15-24	8	26	34	9	30	39	15	21	36
25-34	79	76	155	96	100	196	61	68	129
35-44	118	105	223	211	189	400	222	205	427
45-54	218	199	417	375	339	714	275	287	562
55-64	306	216	522	636	456	1 092	577	478	1 055
65-74	191	163	354	437	421	858	442	445	887
75+	69	69	138	206	234	440	237	268	505
Total	1 015	878	1 891	1 993	1 790	3 783	1 839	1 786	3 625
	Rate per 100 000								
0-14	209	220	215	201	192	197	94	140	117
15-24	123	417	267	139	481	307	202	296	248
25-34	1 296	1 218	1 262	1 574	1 595	1 584	1 080	1 191	1 136
35-44	2 177	1 841	2 005	3 894	3 313	3 596	3 496	3 049	3 266
45-54	3 096	2 575	2 823	5 325	4 387	4 834	4 946	4 678	4 805
55-64	4 746	2 846	3 722	9 768	6 063	7 782	8 324	6 134	7 165
65-74	5 358	3 220	4 103	12 258	8 317	9 946	11 823	8 176	9 662
75+	4 [illegible]	[illegible]	3 15[illegible]	[illegible] 811	8 454	10 055	14 558	9 264	11 170
Total	2 106	1 6[illegible]	1 [illegible]	4 135	3 427	3 783	3 843	3 448	3 625

APPENDIX TABLE 20

AVERAGE DURATION OF HOSPITAL TREATMENT IN DAYS AND NUMBER OF HOSPITAL BEDS OCCUPIED BY TUBERCULOSIS PATIENTS

IN BERLIN (WEST) IN 1961

	1961			1962			1963			1964		
	No. of patients	Average duration of hospital treatment (days)	No. of hospital beds occupied per day [b]	No. of patients	Average duration of hospital treatment (days)	No. of hospital beds occupied per day [b]	No. of patients	Average duration of hospital treatment (days)	No. of hospital beds occupied per day [b]	No. of patients	Average duration of hospital treatment (weeks)	No. of hospital beds per 100 [a]
New cases and relapses	87	126	33	92	115	67	68	52	50	94	147	42
Relapses	8	99	5	24	192	14	19	206	12	21	184	12
Chronic bacillary excretors	47	231	33	18	301	17	8	490	12	7	207	4
Cases diagnosed 1960 [c]	104	187	38	80	202	19	17	179	9	1	88	—
Total	246	174	130	224	170	117	112	180	83	123	156	58

[a] The average duration of hospital treatment was always calculated for the year in which treatment was terminated, in cases of repeated admission in a given year, a separate evaluation of the duration of hospital treatment was made in each case and the patient counted twice.

[b] Calculation of the average number of beds required was based on a 90 % rate of occupation.

[c] Cases diagnosed in 1960 or earlier and still infectious during early part of 1961.

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Epidemiological and clinical study of tuberculosis in the district of Kolín, Czechoslovakia

Second report (1965–1972)

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An epidemiological and clinical study of tuberculosis in a district with a population of 100 000 has been in operation in Czechoslovakia since 1960. Its objective is to ascertain the epidemiological situation and long-term trend in respect of tuberculosis in a country with well-established tuberculosis control facilities. This second report presents the results achieved in the period 1965–72 and the epidemiological trend of tuberculosis observed during the 12-year study period. The fundamental control measures adopted during the study included systematic BCG vaccination of the newborn and revaccination of persons aged 14 and 19 years ; mass surveys of the population over 14 years of age by photofluorography ; case-finding among persons with symptoms and in risk groups ; systematic treatment of all persons with active tuberculosis—i.e., supervised inpatient treatment followed by outpatient self-administered regimens ; and radiological and bacteriological follow-up of cases.

The results confirmed that the systematic application of effective treatment throughout the study population was followed by a rapid decline in the prevalence of bacillary tuberculosis, particularly in its chronic form. The incidence of bacillary tuberculosis declined more slowly, because the risk of contracting the disease continued to be high for middle-aged and elderly persons. Indiscriminate photofluorographic surveys of the study population at 3-yearly intervals produced a decreasing yield.

An increasing proportion of noninfected persons among the population is the basic condition for a further decline of tuberculosis. The cost of tuberculosis control can be reduced by strict adherence to rational and economical working methods. Most of the economic indicators analysed fell to less than one-fifth between 1961 and 1972.

The objective of the epidemiological and clinical study of tuberculosis conducted from 1 October 1960 in collaboration with the World Health Organization in the district of Kolín (hereafter referred to as the Kolín study) was to determine the epidemiological situation of tuberculosis and to ascertain to what degree and within what period of time preventive, diagnostic, and therapeutic tuberculosis control measures, applied according to standardized procedures of WHO, would influence that epidemiological situation.

The first report on the Kolín study, by Styblo et al. (1), presented detailed data on the epidemiological situation of tuberculosis in the period 1961–64. The present report gives the results for 1965–72. The data presented in both reports provide an indication of the trend of the tuberculosis situation over the 12-year study period.

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METHODS

The study was operated according to detailed working protocols agreed upon with WHO.

Systematic vaccination of all the newborn against tuberculosis and revaccination of persons aged 14 and 19 years who reacted with an induration of

Table 1. Basic epidemiological parameters of tuberculosis in Kolín district, 1965–72 (per 100 000 inhabitants)

Parameter	1965	1966[a]	1967	1968	1969[a]	1970	1971	1972[a]
Newly detected cases of bacillary pulmonary tuberculosis confirmed:								
by microscopy or microscopy & culture	22	24	9	14	22	11	12	18
by culture only	24	55	36	31	33	20	14	34
Total	46	79	45	45	55	31	26	52
with primarily resistant *M. tuberculosis*	2	—	1	5	1	1	—	2
with *M. bovis*	7	3	1	3	5	—	1	2
Relapses of bacillary pulmonary tuberculosis confirmed:								
by microscopy or microscopy & culture	3	3	5	4	3	5	1	
by culture only	11	7	6	7	4	3	4	3
Total	14	10	11	11	7	8	5	4
Prevalence of bacillary pulmonary tuberculosis confirmed:								
by microscopy or microscopy & culture	34	36	17	22	26	16	13	18
by culture only	39	61	54	35	41	24	19	38
Total	73	97	71	57	67	40	32	56
cases with resistant *M. tuberculosis*	12	9	8	12	7	5	3	4
Prevalence of inactive pulmonary tuberculosis	1 591	1 609	1 624	1 680	1 671	1 663	1 672	1 610
Prevalence of cases with fibrotic lung lesions	3 544	3 594	3 477	3 318	3 235	3 122	2 999	2 929
Extrapulmonary tuberculosis:								
newly detected cases	13	12	16	11	12	15	9	8
confirmed by bacteriological or histological examination	10	9	14	10	10	12	4	6
Mortality from tuberculosis:								
total number of deaths from tuberculosis	10	11	5	2	6	2	3	1
not registered as cases before death	2	6	—	—	2	—	—	—

[a] Mass photofluorographic surveys of the population over the age of 14 years were carried out in 1966, 1969, and 1972.

0–5 mm to 2 TU of PPD 23 with Tween 80 were continued.

Tuberculin tests by the intradermal Mantoux method with a dose of 2 TU of PPD 23 with Tween 80 were performed annually in schoolchildren aged 7, 11, and 14 years. Furthermore, in 1966 one-third of the persons tested in 1961 and one-third of those tested in 1961 and 1963 were retested. The tuberculin test was repeated in 1969 in approximately two-thirds of the population over the age of 14 years.

Mass photofluorographic surveys of the population over the age of 14 years were repeated for the third time in 1966, for the fourth time in 1969, and for the fifth time in 1972. Persons with findings on the miniature films considered as clinically significant were subjected to a chest X-ray with standard size film and to bacteriological examinations for *Mycobacterium tuberculosis*.

Persons registered on account of active or inactive tuberculosis or fibrotic lung lesions had periodic radiological and microbiological examinations.

All patients with active tuberculosis were systematically treated by the daily administration of drugs. While in hospital, patients received a two-drug or three-drug regimen. After discharge, their treatment continued with domiciliary chemotherapy consisting of a self-administered two-drug combination for 18–24 months.

The diagnosis and control of extrapulmonary tuberculosis continued to be conducted on the same lines as before the study. All patients were entered on records and received hospital or ambulatory treatment according to principles similar to those applied for pulmonary tuberculosis.

RESULTS

Incidence of bacillary pulmonary tuberculosis

Active pulmonary tuberculosis was newly detected in 504 persons during the period 1965–72. The diagnosis was confirmed bacteriologically in 379 cases (75%). Subsequent analysis was restricted to the bacteriologically confirmed cases (Table 1).

Out of the 379 cases of bacillary tuberculosis, 220 (58%) were in males and 159 (42%) in females. The great majority of new cases was found in middle-aged and elderly persons (Fig. 1). *M. bovis* was found in 22 (6.1%) cases with isolated and differentiated strains and was five times as common in males as in females. *M. avium* was found in 1 case (0.3%).

Resistance to antituberculosis drugs in newly detected bacillary cases remained at a low level throughout the period 1965–72, amounting on the average to 3.4%. As a rule, only one drug was involved, most commonly isoniazid or streptomycin.

The extent of X-ray lesions was minimal in 151 cases (40%), moderately advanced in 182 (48%), and far advanced in 46 (12%). Tuberculous cavitation was diagnosed in 30% of patients. Bacillary tuberculosis was diagnosed in 270 persons (71%) with a chest film that, prior to the diagnosis of tuberculosis, had been considered as normal and in 109 persons (29%) registered and followed up for fibrotic lesions.

The method by which new cases had been detected was studied separately for patients with a microscopically positive direct sputum smear and for those

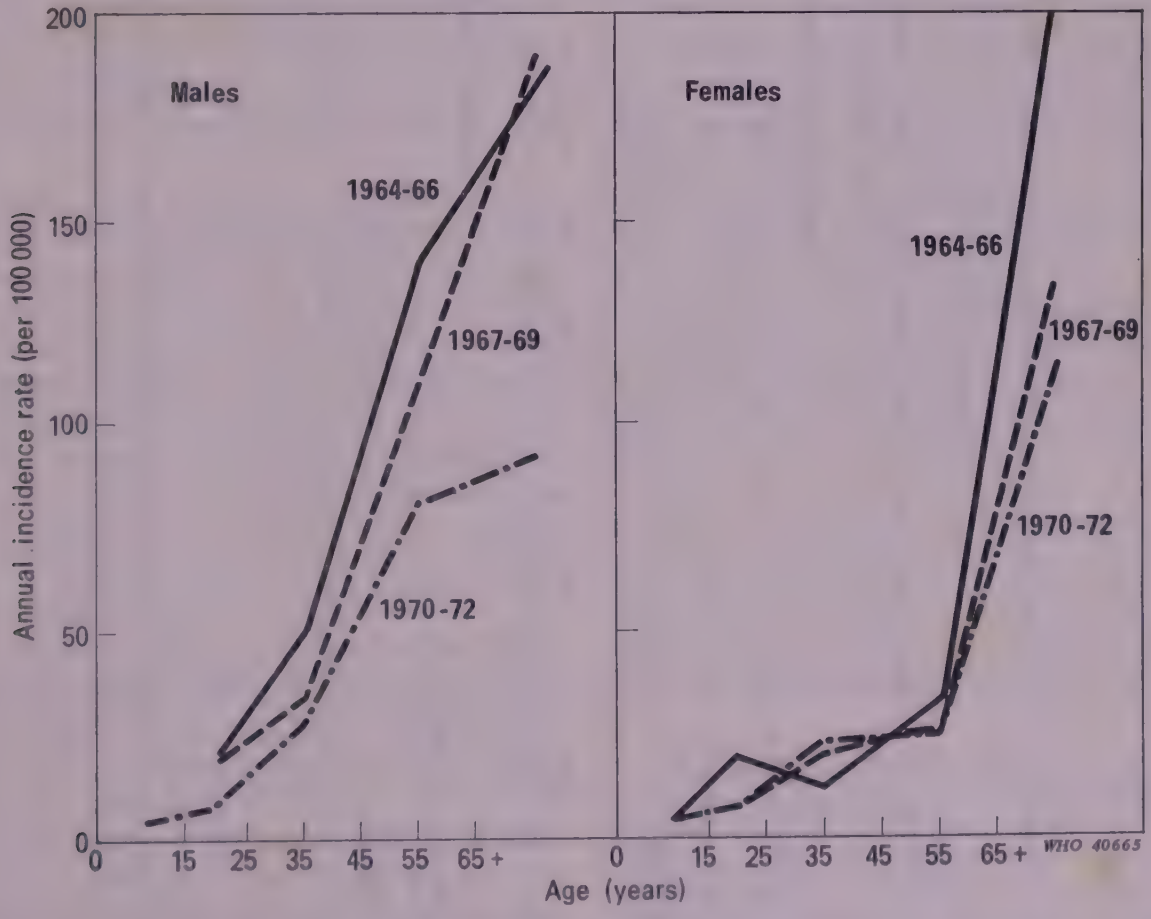

Fig. 1. Average annual incidence rate (per 100 000) of bacillary pulmonary tuberculosis in Kolín district, Czechoslovakia, in 1964–66, 1967–69, and 1970–72, by sex and age.

Table 2. Incidence of bacillary pulmonary tuberculosis in Kolín district, 1965–72, according to method of detection

Method of detection	Cases confirmed by microscopy									Cases confirmed by culture only								
	1965	1966[a]	1967	1968	1969[a]	1970	1971	1972[a]	Total 1965–72	1965	1966[a]	1967	1968	1969[a]	1970	1971	1972[a]	Total 1965–72
Chest X-rays previously evaluated as normal																		
Examination prompted by symptoms	12	5	5	7	8	4	7	8	56	7	4	15	14	4	8	8	13	73
Mass photofluorography	—	14	—	—	11	1	—	4	30	1	33	1	2	19	1	—	15	72
Other preventive examinations	2	1	1	1	—	1	4	2	12	6	4	2	4	3	5	1	2	27
Total	14	20	6	8	19	6	11	14	98	14	41	18	20	26	14	9	30	172
Previously fibrotic lung lesions																		
Examination prompted by symptoms	4	1	2	2	—	3	1	2	15	3	2	7	4	4	2	3	—	25
Regular check-up	4	3	1	4	3	2	—	2	19	7	12	11	7	3	4	2	4	50
Total	8	4	3	6	3	5	1	4	34	10	14	18	11	7	6	5	4	75
Grand total	22	24	9	14	22	11	12	18	132	24	55	36	31	33	20	14	34	247

[a] Mass photofluorographic surveys of the population over the age of 14 years were carried out in 1966, 1969, and 1972.

found by culture only to be excreting tubercle bacilli (Table 2). Mass photofluorographic surveys of the population over 14 years of age, repeated three times (1966, 1969, and 1972), with a total of approximately 200 000 X-ray examinations, disclosed only 30 patients positive on microscopy and 72 patients positive on culture.

Out of the 270 patients with bacillary tuberculosis newly detected during the period 1965–72, 241 had been subjected to photofluorography before the study and 29 (1 immobile person and 28 persons newly resident in Kolín) had not. Among the 241 new cases whose photofluorographic films were available, 208 had their originally negative findings confirmed at the reevaluation, whereas in 33 (14%) a fresh evaluation of their previous films revealed that minimal lesions had been missed or erroneously interpreted in the first instance.

Analysis of the data on BCG vaccination and tuberculin allergy in the group of 208 cases with negative X-ray findings on admission to the study showed that 24 persons had been previously vaccinated with BCG—13 of them with Danish vaccine in 1948 or 1949. In the remaining 184 cases, the data on tuberculin allergy in 1961 indicated that 9 persons had shown an induration of 0–5 mm to 2 TU of PPD with Tween 80; 11 had an induration of 6–11 mm; and 146 had an induration of 12 mm or more. Eighteen persons had not been tested with tuberculin.

Detailed analysis of the previous radiological records for all newly detected cases made it possible to determine with considerable accuracy the incidence of bacillary tuberculosis in the district under study during each period culminating in a mass photofluorographic survey. The incidence during the period 1964–66 had an annual mean of 31.5 per 100 000 of the population; in 1967–69 it was 27.6; and in 1970–72 it was 26.2. Males accounted for 59% of the incidence and females for 41%. The age distribution of these patients was similar to that for all newly detected cases.

In a series of 208 persons whose disease had developed during the period 1965–72, the interval that had elapsed from the last negative photofluorographic film up to the date of diagnosis of bacillary tuberculosis was evaluated. In 19 (8%), the disease developed within one year. In as many as 99 persons (42%), bacillary tuberculosis was found within 2½ years; no significant difference was observed between cases confirmed by microscopy and those verified by culture only.

Relapses of pulmonary tuberculosis [a]

During the period 1965–72 relapses occurred in 84 persons; in 70 (83%) of these, bacteriological confirmation was obtained (Table 1). A bacillary relapse occurred in 42 males and 28 females. *M. bovis* was isolated from one of the patients. Resistant tubercle bacilli, mostly against isoniazid alone, were present in 7 patients (10%).

Tuberculosis of minimal extent was found in 16 cases (23%); in 39 (56%) the disease was moderately advanced, and in 15 (21%) it was far advanced. Cavitation was found in 30 patients (43%).

Symptoms drew attention to the relapse in half of the cases (36); in the remainder, relapse was detected during annual radiological and bacteriological checks (30 cases) or only at necropsy (4 cases).

Prevalence of bacillary pulmonary tuberculosis [b]

The prevalence of bacillary tuberculosis amounted to 73 per 100 000 in 1965 and to 56 in 1972 (Table 1; Fig. 2), males accounting, on the average, for 63% of the prevalence for the entire period and females for 37%. The peak of the age distribution curve was the 65–74-year age group for males and the group over 75 years of age for females.

The main mass of prevalence was supplied by new cases: 44 in 1965 and 49 in 1972. The subgroup of relapses numbered 11 in 1965 and 4 in 1972. The prevalence of chronic excretors of tubercle bacilli, which was 8 per 100 000 in 1965, declined to zero in 1972. The number of chronic excretors was reduced as a result of 6 deaths and 2 cases of sputum conversion (Table 3).

The percentage of patients who excreted drug-resistant tubercle bacilli (generally to only one drug) fluctuated during the period 1965–72 between 7% (1972) and 18% of the prevalence of bacillary tuberculosis.

Prevalence of inactive pulmonary tuberculosis

The prevalence of inactive pulmonary tuberculosis amounted to 1 591 per 100 000 in 1965 and rose to 1 680 in 1969 (Table 1), a slight decline being observed during the ensuing 4 years (1 610 in 1972)

[a] Bacteriological or radiological evidence of active tuberculosis in persons registered as having inactive tuberculosis was held to indicate a relapse.

[b] The prevalence of bacillary tuberculosis is defined as the number of cases of pulmonary tuberculosis in which the excretion of tubercle bacilli has been found by bacteriological examination (direct microscopy, culture, or biological investigation) to have occurred at least once during the past 12 months.

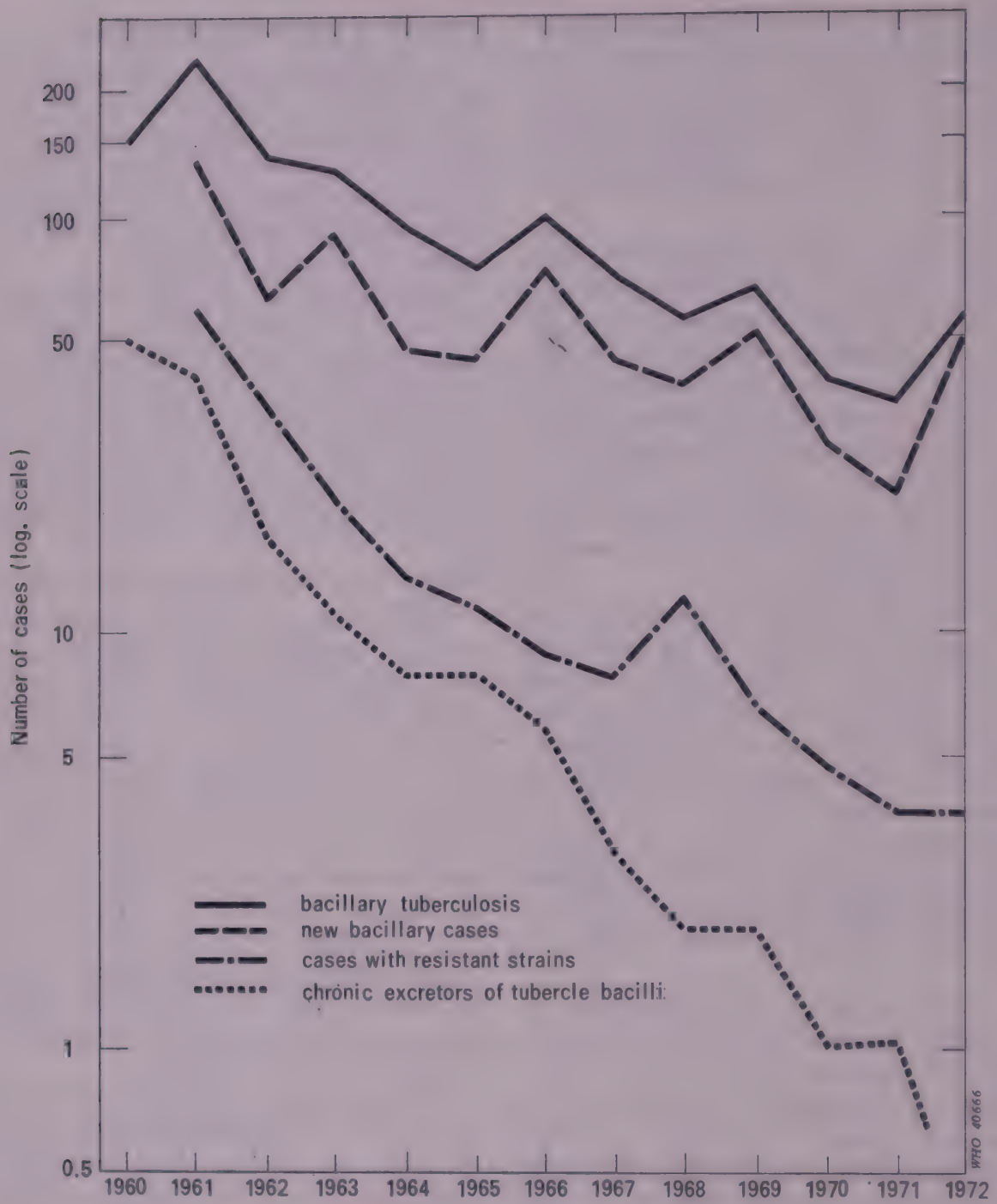

Fig. 2. Prevalence of bacillary pulmonary tuberculosis, new bacillary cases, cases with resistant strains, and chronic excretors of tubercle bacilli, 1960–72.

since the natural reduction of persons with inactive tuberculosis exceeded the number of persons transferred to this group.

Prevalence of persons with fibrotic lung lesions

The prevalence of cases with fibrotic lung lesions amounted to 3 544 per 100 000 in 1965 and 2 929 in 1972 (Table 1). It declined during the period 1965–72 by 615, mainly as a result of natural reduction by death.

In contrast to the prevalence of active and inactive tuberculosis, that of cases with fibrotic lesions was almost identical for males and for females.

Extrapulmonary tuberculosis

New cases of extrapulmonary tuberculosis were diagnosed in 96 persons (32 males and 64 females) during the period 1965–72 and in another 4 only at necropsy (Table 1). More than three-quarters (79%) of these cases occurred in age groups over

Table 3. Prevalence rate (per 100 000 inhabitants) of bacillary pulmonary tuberculosis in Kolín district, 1965–72, according to type of disease [a]

Group	Prevalence rate							
	1965	1966	1967	1968	1969	1970	1971	1972
Newly discovered cases	44 (21)	73 (23)	44 (8)	38 (13)	52 (19)	28 (10)	21 (9)	49 (16)
Relapses	11 (3)	8 (3)	10 (5)	10 (4)	7 (3)	5 (3)	5 (1)	4 (1)
Chronic excretors of bacilli	8 (6)	6 (4)	3 (2)	2 (2)	2 (2)	1 (1)	1 (1)	—
Remainder	10 (4)	10 (6)	14 (2)	7 (3)	6 (3)	6 (2)	5 (2)	3 (1)
Total	73 (34)	97 (36)	71 (17)	57 (22)	67 (26)	40 (16)	32 (13)	56 (18)

[a] The number of cases found by direct microscopy is given in parentheses.

45 years. Extrapulmonary tuberculosis was confirmed by bacteriology in 35 patients (36%). Histological examination of specimens bore out the diagnosis of tuberculosis in another 40 cases (42%). Disease caused by *M. bovis* occurred in 3 patients.

The most common site of extrapulmonary tuberculosis in both males and females was the subcutaneous lymph nodes (33 patients). Other sites affected were the bones and joints (26 cases), the urinary tract (14 cases), the skin (7 cases), the genital organs (9 cases), and the intestines and liver (7 cases). Tuberculous meningitis was diagnosed in 3 patients, aged 26, 51, and 75 years—in one of them only at necropsy.

Mortality from tuberculosis

During the period 1965–72 a total of 40 persons, some of whom had been previously registered as patients and others not, died from tuberculosis. Of these, 25 were men and 15 were women (Table 1). Mean mortality from tuberculosis was 8.7 per 100 000 during the period 1965–67, 3.3 during 1968–70, and 2.0 during 1971–72. None of those who died from tuberculosis was under the age of 40 years; 21 were between the ages of 41 and 70 years, and 19 were over 70 years.

Despite the systematic programme of case-finding in operation, a number of previously unknown cases were diagnosed only at necropsy. During the period 1965–72, there were 10 such cases (4 men and 6 women), i.e., one-quarter of all deaths from tuberculosis. About one-quarter of the bodies of deceased persons were subjected to necropsy each year in Kolín district, especially persons who died in hospital.

The epidemiological impact of treatment

Chemotherapy of tuberculosis was conducted throughout the entire period according to the Kolín study protocol drafted in 1960. Daily uninterrupted combined therapy was used.

The long-term treatment results were evaluated in 649 persons with newly detected bacillary tuberculosis and 141 persons with a relapse confirmed by bacteriology during the period 1961–70. These had been under observation for periods of 2–12 years before the target date of 31 December 1972. Relapse occurred in 15 patients, the average annual risk of relapse being 0.6% (expressed as a percentage of patient-years). A further treatment failure was recorded in 4 persons, i.e., in 0.5% of the total study population; these patients developed a chronic form of tuberculosis.

In addition, the cases of 70 chronic excretors of tubercle bacilli, who also had been treated during 1961–72 according to the study protocol, were evaluated. Sputum conversion was achieved in 43 persons (61%); 27 (39%) died without sputum conversion. A relapse occurred in only one of the chronic excretors under study.

Epidemiological trend of bacillary pulmonary tuberculosis, 1961–72

The trend of the epidemiological situation as regards tuberculosis was evaluated for the period 1961–72. The most remarkable decline was observed in the prevalence of bacillary tuberculosis, which dropped from 233 per 100 000 in 1961 to 56 in 1972. The mean annual decline amounted to 12.9% and was statistically highly significant (Fig. 2).

The most rapid reduction occurred in the subgroup of chronic excretors of tubercle bacilli, whose prevalence declined from 40 per 100 000 in 1961 to 17 in 1962 and to zero in 1972. The average annual decline of the prevalence curve was 31.9%.

The prevalence of cases with tubercle bacilli resist-

ant to one or more antituberculosis drugs declined from 59 per 100 000 in 1961 to 36 in 1962 and to 4 in 1972. Resistant cases formed 27% of the prevalence in 1961, 25% in 1962, and 7% in 1972. Their average annual decline was 20.5% and was statistically highly significant.

The incidence of bacillary tuberculosis decreased from 142 per 100 000 in 1961 to 52 in 1972. The mean annual reduction amounted to 9.4% and was statistically significant (not shown in Fig. 2).

Economic aspects

Evaluation of the economic indices of tuberculosis control, mentioned by Stýblo et al. (1) in the report for 1961–64, was continued during the period 1965–72. The indices can be assessed objectively and their trends can be compared throughout the 12-year duration of the study. The study related to the average number of beds for the treatment of tuberculosis, the number of patients given chemotherapy on an outpatient basis, the amount of drugs prescribed, the number of days of incapacity for work, and the number of new disablement pensions granted on account of tuberculosis.

The average number of beds used for the treatment of patients suffering from tuberculosis was 40 in 1965 and 17 in 1972. The number of outpatients receiving chemotherapy in the district of Kolín was 115 in 1965 and 73 in 1972. The amount of isoniazid prescribed in the period 1965–72 decreased from 15 kg in 1965 to 6 kg in 1972, that of streptomycin from 5 kg to 3 kg, and that of PAS from 390 kg to 81 kg. The consumption of ethionamide and pyrazinamide showed a similar trend. Little use was made of other antituberculosis drugs.

Because of the declining number of new cases and relapses found in employees, the number of working days lost on account of tuberculosis decreased during the 8-year study period. In 1965 there were 7 802 days of incapacity for work due to tuberculosis, and in 1972 there were 4 409 days. The average duration of incapacity varied very little between years because the criteria for evaluating incapacity remained unchanged during the whole period of the study.

A full or partial disablement pension because of tuberculosis was granted to three persons in whom tuberculosis was diagnosed in 1965.

Evaluation of the trend of the given indices for the 12-year period 1961–72 shows that the most radical decrease was achieved in the first 4 years; subsequently the decline became more gradual.

DISCUSSION

Since this report is a continuation of the previously published article by Stýblo et al. (1), it has been possible not only to evaluate the results attained in the past 8 years (1965–72) but also to estimate how far the objectives of the study were met in the whole 12-year period (1961–72) during which the study was uniformly conducted according to the original protocol.

A 12-year follow-up of the epidemiological situation of tuberculosis in a district with 100 000 inhabitants supplied the answers to most of the questions raised at the start of the study. The study demonstrated that, in an area in which the young population had for a long time been systematically vaccinated against tuberculosis, so that the incidence and prevalence of tuberculous infection could not be studied, the epidemiological situation could be evaluated according to the incidence and prevalence of bacillary pulmonary tuberculosis—i.e., tuberculosis confirmed chiefly by microscopy. The long-term study of the trends of incidence and prevalence of tuberculosis has laid the foundations for rational changes in tuberculosis control.

The epidemiological trend of tuberculosis

The decline in the prevalence of bacillary pulmonary tuberculosis, which was 12.9% annually on the average, showed the effectiveness of the treatment used. The speed of the decline in the number of patients varied in the different subgroups of prevalence. The most rapid decline was observed in chronic patients, significant results having been reported by Křivinka et al. (2) after 3 years of the study. A further sputum conversion in the remaining chronic patients was difficult to attain. Towards the end of the 12-year period only one-third of the original number of such patients were still alive and not excreting bacilli, whereas two-thirds had died, from tuberculosis or from other diseases. The number of chronic patients was limited, to some extent on account of specific treatment but chiefly because the effective treatment of new cases and relapses had prevented the development of new chronic cases. Chronic tuberculosis developed in only 4 of the cases detected and treated in the study. Sputum conversion in such cases is expensive and the greatest possible effort should therefore be made to avoid the development of the chronic form of tuberculosis.

The remaining two subgroups—new cases and relapses—were less responsible for the decline in prevalence. In tuberculosis relapses their absolute

and relative number declined in keeping with the increase—in the group of inactive tuberculosis—of persons treated according to the protocol of the study.

The incidence of bacillary pulmonary tuberculosis declined by 9.4% per year. Most cases developed in middle-aged and elderly persons. In an area where a high proportion of the population in these age groups has been infected by tuberculosis, the decline in incidence cannot be speeded up considerably for the time being. Bovine infection played a considerable role in the infection of the population, as shown by the fact that 6% of patients with new bacillary tuberculosis were excreting *M. bovis*. Several cases caused by this mycobacterium occurred also in the years following the elimination of bovine tuberculosis in 1968.

Sporadic but advanced cases of bacillary tuberculosis, positive by microscopy, occurred even after 12 years of careful tuberculosis control. Their insidious nature was evident from the fact that some of them were diagnosed only at autopsy.

The epidemiological importance of treatment

The treatment of known cases of bacillary tuberculosis does not, as a rule, present any insuperable problems in cooperative patients. Despite the known objections—referred to by Fox (3)—that could be raised on the basis of present knowledge against the system of treatment employed in the study, good results were obtained. In only 16 persons—i.e., in 0.6% annually, did bacteriologically confirmed tuberculosis relapses occur. The treatment method used proved to be an effective part of the tuberculosis control programme, leading to a favourable development of the epidemiological situation.

The risk of tuberculosis in different population groups

The epidemiologically most important risk groups increasingly appear to be men over 45 years of age infected with tuberculosis and women over 65 years of age infected with tuberculosis. These groups will continue to present a serious risk, but the lower age limit in men will gradually rise.

In the first 4 years of the study, further risk groups had already become apparent—i.e., persons who had had tuberculosis, particularly those who had not been adequately treated, and persons with fibrotic lesions in the lungs. The subsequent 8 years fully confirmed the importance of these two risk groups.

The risk of tuberculosis in persons—chiefly children and young people—in contact with the disease could not have been studied in detail owing to the small number of such persons.

Methods of tuberculosis control

Undoubtedly BCG vaccination played an important role at a time when many human and animal sources of infection existed in the population. During the study the vaccination of newborn infants was continued. The main reason for not postponing vaccination of children to a later age is the fact that vaccination of the newborn gives fairly reliable protection against tuberculous meningitis and other disseminated forms of tuberculosis in infancy. However, BCG vaccination is becoming an obstacle to the use of tuberculin tests for diagnostic purposes, and this offsets its benefits. Furthermore, immunity as a result of BCG vaccination is not of unlimited duration, as was demonstrated by the Medical Research Council of Great Britain (4) and by Guld et al. (5).

Microscopic examination of the sputum is acquiring increasing importance for the rapid diagnosis of sources of infection, for rapid orientation regarding the efficacy of drugs, and for providing data suitable for international comparison.

It appears that radiophotographic detection of tuberculosis requires an entirely new approach. The study demonstrated with accuracy that indiscriminate case-finding performed in persons over 15 years of age at 3-year intervals was of little value in the conditions of the Kolín study. The detection of one case of bacillary tuberculosis by radiophotography was expensive. However, detection is difficult without radiophotography since approximately one-half of new patients have no symptoms. That is why it is necessary to focus attention on the detection of cases among persons with a high tuberculosis incidence and among those complaining of symptoms.

When the tuberculosis infection rate in the population is as high as it was in Czechoslovakia in the past, the elimination of the disease is laborious and costly, besides being a long-term task in view of the insidious and chronic nature of tuberculosis and its possible endogenous exacerbation. Tuberculosis control in human beings must proceed in conjunction with the eradication of tuberculosis in cattle.

When the results of the study were evaluated after it had been in progress for 12 years, it became clear that the expense incurred in conducting it had been a good investment. Most of the economic indices studied were reduced during the 12 years to less

than one-fifth. Moreover, the study provided valuable documentation for the planning of health services. Tuberculosis will demand attention for many more years, but the extent of these activities will diminish. The Kolín experience shows that it is possible to reduce the tuberculosis problem gradually, but only through systematic work over a long period.

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RÉSUMÉ

ÉTUDE ÉPIDÉMIOLOGIQUE ET CLINIQUE DE LA TUBERCULOSE DANS LE DISTRICT DE KOLÍN (TCHÉCOSLOVAQUIE): DEUXIÈME RAPPORT (1965-1972)

L'enquête sur la tuberculose menée avec la collaboration de l'Organisation mondiale de la Santé au sein d'une population de 100 000 habitants dans le district de Kolín, en Tchécoslovaquie, a débuté en octobre 1960. Ce deuxième rapport expose les résultats enregistrés durant la période 1965-1972 et résume l'essentiel des observations faites pendant les 12 premières années de l'étude.

De 1965 à 1972, on a découvert au total 379 nouveaux cas de tuberculose bactériologiquement confirmés, dont 58% parmi des hommes et 42% parmi des femmes. Dans leur grande majorité, il s'agissait d'hommes de plus de 45 ans et de femmes de plus de 65 ans.

Dans 93,6% des nouveaux cas, la maladie était causée par *Mycobacterium tuberculosis*, dans 6,1% par *M. bovis* et dans 0,3% par *M. avium*. On n'a constaté qu'un faible taux de pharmacorésistance primaire, 3,4% en moyenne pour la période 1965-1972, ne concernant généralement qu'un seul médicament.

Parmi les nouveaux cas, 270 (71%) n'avaient présenté auparavant aucune image radiologique suspecte, tandis que les 109 autres (29%) avaient été reconnus atteints de lésions pulmonaires fibreuses et placés sous surveillance. Trois campagnes de radiophotographie de masse de la population âgée de plus de 14 ans, comportant environ 200 000 examens radiologiques, n'ont fait découvrir que 30 malades positifs à l'examen microscopique et 72 malades positifs à la culture.

Les 270 nouveaux malades dépistés ont fait l'objet d'une analyse détaillée portant sur la vaccination antérieure au BCG, l'allergie tuberculinique et les antécédents radiologiques. La vaccination avait été pratiquée chez 24 d'entre eux, et chez 13 déjà en 1948-1949 par le vaccin danois. Seuls 5% des sujets du groupe non vacciné présentaient une induration de 0-5 mm à l'épreuve tuberculinique au début de l'enquête.

Des lésions tuberculeuses ont été découvertes chez 42% des malades moins de 2½ ans après un examen radiologique négatif, ce qui tend à minimiser l'importance de la radiophotographie pratiquée à intervalles de 3 ans.

De 1965 à 1972, des rechutes de tuberculose pulmonaire avec confirmation bactériologique sont survenues chez 42 hommes et 28 femmes. Elles ont été plus fréquentes dans les groupes d'âge élevé. On a isolé dans un cas *M. bovis*. Des bacilles tuberculeux résistants, pour la plupart à l'égard de l'isoniazide seul, ont été trouvés chez 7 malades.

La prévalence de la tuberculose pulmonaire confirmée a été en 1965 de 73 et en 1972 de 56 pour 100 000, le sexe masculin étant atteint dans la proportion de 63%, pendant l'ensemble de la période. La prévalence des malades excrétant chroniquement des bacilles est passée de 8 en 1965 à 0 pour 100 000 en 1972.

On a enregistré 40 décès par tuberculose pulmonaire pendant la période 1965-1972. Le taux moyen de mortalité a atteint 8,7 en 1965-1967 et 2,8 pour 100 000 en 1968-1972. De 1962 à 1972, la réduction moyenne annuelle de la prévalence de la tuberculose pulmonaire s'est élevée à 12,9%, valeur statistiquement significative. Le déclin le plus rapide a été observé dans le groupe

des excréteurs chroniques de bacilles. La réduction moyenne annuelle de l'incidence, statistiquement significative, a été de 9,4%.

L'étude a fait ressortir que le coût de la lutte antituberculeuse peut être abaissé si des méthodes de travail rationnelles et économiques sont strictement appliquées. La plupart des indicateurs économiques qui ont été analysés — besoins journaliers en lits d'hôpitaux pour le traitement des malades tuberculeux, nombre de malades traités ambulatoirement, quantité de médicaments requise pour les traitements hospitaliers et ambulatoires, etc. — ont vu leur valeur décroître de plus des 4/5 de 1961 à 1972.

Il a été démontré que la prévalence de la tuberculose peut être influencée par la chimiothérapie. La survenue de nouveaux cas dans les groupes d'âge élevé et leur dépistage posent encore quelques problèmes. Dans la région de l'enquête, où les sources de contagion tuberculeuse sont peu nombreuses, le pourcentage croissant de personnes non infectées et de sujets vaccinés est une condition importante de l'évolution favorable de la maladie.

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